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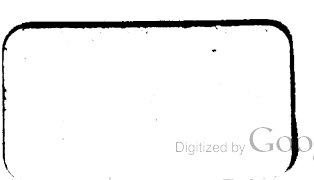

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Practical Medicine Series

COMPRISING TEN VOLUMES ON THE YEAR'S PROGRESS IN MEDICINE AND SURGERY

UNDER THE GENERAL EDITORIAL CHARGE OF

CHARLES L. MIX, A. M., M. D.

PROFESSOR OF PHYSICAL DIAGNOSIS IN THE NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

VOLUME IX

SKIN AND VENEREAL DISEASES

EDITED BY

OLIVER S. ORMSBY, M. D.

PROFESSOR AND HEAD OF THE DEPARTMENT OF SKIN AND VENEREAL DISEASES, RUSH MEDICAL COLLEGE

AND

JAMES HERBERT MITCHELL, M. D.

HYDE MEMORIAL FUND FELLOW, ASSISTANT IN CUTANEOUS PATHOLOGY, RUSH MEDICAL COLLEGE

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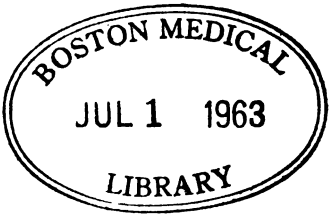

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INTRODUCTION.

Either as a direct or indirect result of the war a number of events of importance have transpired during the past year. Among the former may be mentioned the passage of the "Trading with the Enemy Act" which will preclude any further importation of salvarsan during the war, and the granting of a license to American laboratories to manufacture the drug. Another direct result is the disappearance of all German medical journals from circulation in this country. Various journals have been brought into the United States, but they have not been available for the purposes of this volume and hence the absence of all references to German medical literature except a few which were too late for the 1916 volume.

An indirect result of the war has been the creation of new journals, published in our own country and in our own tongue to fill the gap made by the disappearance of the publications of the Central Empires. Among these new journals, two, namely, the *Journal of Immunology* and the *American Journal of Syphilis,* are valuable additions to our literature.

In the dermatological contributions for the year are to be found a new dermato-mycosis, a rare form of neoplasm first described by Schweninger and Buzzi; a study of the eruption caused by an animal parasite, *Demodex folliculom,* hitherto considered non-pathogenic for man; a description of a case of generalized blastomycosis without cutaneous lesions; and careful studies, experimental and clinical, of the metabolism in eczema and eczematoid dermatitis; of Barcoo rot, perleche, and primrose dermatitis. New and apparently valuable methods of treatment for leprosy and granuloma venereum are described.

From the dermatologists in military service have come interesting papers setting forth the diseases they are called upon to treat, and the military methods of com-

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bating pediculosis and scabies. For the latter, two new methods of treatment are described, one of which makes use of chlorine and the other of sulphur dioxide gas. As a result of extensive observations in the field it has been demonstrated that *Pediculus vestimentorum* does not always deposit its eggs in the clothing, but may attach its eggs to the pubic hair.

The eruptions due to the handling of tetryl, and to contact with a peculiar substance dropped in bombs in raids on London have been well described.

Considerable attention has been devoted to the sociologic and economic side of the venereal disease problem. Extensive work in routine Wassermann examinations in various institutions has been carried on, and the value of the routine Wassermann test has been clearly demonstrated. In military surgery, the Wassermann reaction has given valuable information in clearing up doubtful diagnoses.

In the technique of the Wassermann reaction several new modifications have been described and various improvements upon existing methods have been reported.

In the treatment of syphilis the worthlessness of sodium cacodylate and venarsen have been proved. Vanadium has now been added to the list of drugs of value in the treatment of syphilis.

THE EDITORS.

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SKIN AND VENEREAL DISEASES.

DERMATOSES.

General Considerations.

Nitrogen Metabolism of Eczema. In a previous communication[1] Schamberg and Raiziss[2] showed that the nitrogenous metabolism in psoriasis presents considerable deviation from that of normal individuals. In practically all the cases which they studied there was evident a marked tendency to store up nitrogen in the body. In severe cases, the amount of nitrogen retained was most striking; the elimination of nitrogen in the urine was in certain cases depressed to the lowest level ever recorded either in normal or pathologic conditions. Their studies and experiments demonstrated that a low nitrogen diet had, in general, a favorable influence on the course of the eruption, and, *per contra,* that a high nitrogen diet exerted an unfavorable influence on the cutaneous condition.

The authors have now been instituting metabolic studies in cases of eczema and other eruptive diseases characterized by marked exfoliation of the epithelial cells in order to compare the results with their findings in psoriasis. In this communication are presented the results of a prolonged metabolic study of two cases of eczema.

One was a case of chronic eczematoid dermatitis of external origin which should properly be excluded from the category of eczema, and which differed from the other case in history, symptomology, metabolic picture and response to treatment.

The analysis of the results obtained in the metabolic

(1) Practical Medicine Series, Vol. IX, 1914.
(2) Jour. Cut. Dis., March, 1917.

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PLATE I.

Eczematoid dermatitis simular to Case I. discussed by Schamberg and Raiziss (see page 5).
(Case in photographic series of Ormsby and Mitchell.)

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this substance and under favorable condition at least to conserve the acquired amount of extra nitrogen.

No relationship was found to exist between the retention or loss of nitrogen and the weight of the patients. Patient No. 1, for instance, lost considerable weight during the first periods, whilst at the same time a gain of nitrogen occurred; the same patient during certain periods lost large amounts of body nitrogen without any change in weight. Patient No. 2 retained nitrogen throughout the entire period of observation, yet lost in weight. In their studies of psoriasis the authors called particular attention to this same disproportion between nitrogen retention and change in body weight.

The course of the two types likewise differed widely.

Case 1 was kept on a low nitrogen diet for five weeks without any influence being observed upon the course of the eruption or upon the associated itching.

In Case 2, on the other hand, the patient was markedly benefited under low nitrogen dietary and placed in a condition better than he had been in twenty months.

A hasty consideration of these results might convince one of the discrepant influence of a low nitrogen diet in eczema. But a more careful study of these two cases, from various points of view, leads to some most interesting and suggestive deductions.

In the first place it is obvious to any one who reads the description of the eruption and histories of these patients that these two individuals were suffering from separate and distinct diseases. In the still incomplete state of our knowledge of eczema, we are unquestionably placing in this category a variety of disorders having certain symptoms in common, but which are diverse and distinct in their etiology and essential nature.

In Case 1 the patient was an ignorant laborer, lacking all self control, who had a dermatosis of two months' duration, which began as chapped hands while working in the cold, and which continued to grow worse under the influence of unrestrained scratching. There was never any vesiculation or serous exudation, but merely redness, scaling and thickening of the skin. This condition, therefore, is not a true eczema, but a chronic dermatitis due to external irritation.

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In Case 2, on the other hand, the patient was a man, 29 years old, who has suffered from outbreaks of an eruptive disorder since the age of two years. For the greater part of his life he has been subject to a skin trouble whose chief characteristics are vesicle formation, surface exudation and itching. The eruption would develop suddenly and on rare occasions was preceded by chilliness and fever, an unusual phenomenon.

In its essential features this affection is eczema in its orthodox sense, a boiling over. There can be no doubt that this disease in this patient is of systematic origin. It is obviously not a skin affection of external causation.

In Case 1 the patient was unable to maintain a nitrogen balance on a low nitrogen diet (from 4 to 5 grams a day). During a period of forty days he lost 87 grams of nitrogen. Although the large amount of scaling and loss of epithelium suggested a condition similar to that which occurs in psoriasis, his nitrogen metabolism was quite unlike that which occurs in this disease, for psoriatic patients retain nitrogen even on a low nitrogen diet.

In Case 2, on the other hand, the man retained nitrogen on a low nitrogen dietary and presented a metabolic picture like that of psoriasis patients, although clinically, of course, there was not the slightest resemblance.

It is a most significant and interesting observation that a prolonged low nitrogen diet exerted no favorable influence at all in Case 1, in which the patient showed no nitrogen retention, but on the contrary, did markedly benefit the patient in Case 2, who gave evidence of a pronounced nitrogen retention. The improvement was gradual and progressive, quite like that observed in psoriasis patients.

The patient with chronic dermatitis eliminated "rest nitrogen" in distinct excess of normal for a long period of time, but the elimination of "rest nitrogen" in the case of eczema did not exceed the maximum normal limits. The elimination of creatinine in both patients was normal. Both patients exhibited an increase in the elimination of endogenous uric acid, the case of chronic dermatitis showing the higher figures. The uric-acid content of the blood, however, was normal. The increased

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uric-acid output is not to be interpreted as an indication of gout, but doubtless bears some relation to the leukocytic deposits in the skin with, perhaps, absorption of some of the products of the same.

Relation of Primrose Dermatitis to Anaphylaxis. An excellent piece of experimental work has been carried out by C. A. Simpson,[3] showing that the toxic substance of the primrose is neither an oil nor a protein, and being non-protein in nature it can not cause anaphylaxis.

Primula obconica seems to have been imported into Europe from China in 1883. Several years later it made its appearance in America, and since then several dermatologists in this country have made it and its resulting dermatitis the subject of some interesting papers. Foerster, Zeisler and Montgomery especially have given excellent reports and clinical data of cases under their observation. All of them, however, rely on one article (Nestler's) for their analysis of the poisonous principle of the plant. Nestler was more or less of a pioneer, and though his observations were good, so far as they went, his analysis was most superficial and limited. He did not say that the active poison was an oil, as some American abstractors imply and quote him as saying. He confined his description in this regard to what he termed poisonous material, which he repeats several times in his article, and then goes on to mention its solvents.

Nestler was under the impression that every one could be poisoned by the primrose, and after many efforts succeeded in producing a dermatitis on himself. He did recognize a varying sensibility of different individuals, however, and suggested its relation to the reaction of anaphylaxis.

In Simpson's cases of primrose dermatitis there was lack of well-marked isolated areas of intense irritation and vesiculation with the outline of the twig and leaf, such as one sees in rhus poisoning. Rather is the irritation of a more irregular, diffuse, ill-defined, erythematous character. As a result of this apparent difference in the irritability of the two poisons, the sufferers from primrose dermatitis seldom complain of pain, ten-

(3) Jour. Amer. Med. Ass'n., July 14, 1917.

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derness and irritation which one sees in rhus poisoning. On the other hand, the subjective symptoms of itching, however, appear to be much more intense in primrose dermatitis. In addition to this annoying symptom, the patient soon begins to show signs of irritability from lack of sleep and rest. To add to the injury, a number of Simpson's cases had been diagnosed as scabies and so liberally anointed with sulphur ointment as to complicate the picture with a sulphur dermatitis.

There is nothing difficult in the diagnosis. The dermatitis, which is usually limited to the hands, lower arms and the face, strikes one as being entirely artificial. In any vague cutaneous irritation involving the above-mentioned locations, one should always inquire if the sufferer handles or comes in contact with flowers. As to be expected, the removal of the source of irritation soon terminates the outbreaks, and a soothing zinc and tragacanth lotion with some such antipruritic as phenol (carbolic acid) or menthol relieves the itching and heals the lesions.

Considering the frequency of primrose dermatitis, it is rather odd that so little has been done in the search for the exciting poison. A comparison of the literature on this lesion with that dealing with rhus poison emphasizes this very clearly. The work of Syme and Ford in regard to this form of dermatitis venenata deserves praise, although the work of both has since been refuted. Syme was no doubt dealing with more than a simple glucoside, while Ford's attractive immunity and antitoxin theory built on his idea that glucosides produce specific antibodies, has been attacked from several directions.

Without any knowledge of the active principle of the plants, it is doubly hard to understand their mode of action. This lack of knowledge has given rise to many hypotheses, of which anaphylaxis has been the most frequently suggested.

The lack of information on primrose poison can only be compared with the confusion which has arisen over the mode of action of this and other poisons. The known susceptibility and immunity of certain persons to these substances so frequently observed by dermatol-

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ogists are so imperfectly understood that they are apt to be confused with other reactions.

In order to show experimentally that primrose dermatitis does not depend on the general irritability of the skin, a reaction such as one often sees in some patients after the application of almost any degree of traumatic or chemical irritant, Simpson applied a leaf of the plant to the arm of a patient who was in the midst of an attack of urticaria and who not infrequently suffered from an idiopathic eczema. Twelve hours later there was no sign of dermatitis or irritation, and the outline of the leaf on the skin was barely noticeable.

Simpson then attempted to produce active and passive anaphylaxis in two guinea-pigs by an intraperitoneal injection of a sensitizing salt solution extract of the primrose; in two other pigs, the sensitizing injection was composed of serum obtained from one of the susceptible patients. Five days later he reversed the injections, this time giving the serum to the primrose animals and the primrose to the serum animals. In one other animal, both the sensitizing and anaphylactic intraperitoneal injections, at five-day intervals, were of primrose extract. In this work only one of the animals died or showed signs of shock the day the second injection was given. On repetition of the test on another pig, however, the animal lived three days and died not of shock but from actual plant poison, as was shown by the presence of an indurated abdominal lesion similar to that which Ford found in his animals after injecting rhus extract.

In an effort to learn the part played by the plant protein in the dermatitis, Simpson prepared an extract of the leaves which gave the Millon test for protein. He inoculated a concentrated extract of this precipitate into two scarified areas on the arms of two susceptible patients, who were kept under observation for ten days. During this time neither patient experienced the slightest subjective or objective symptom of a skin reaction. On another lot of leaves he made an effort to isolate an alkaloid, but was unsuccessful. A crude glucoside and an oleoresin were isolated, both of which proved to be intensely irritating to susceptible patients.

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There are, therefore, most probably two active poisons in *Primula obconica,* one obtained by precipitating an extract with litharge and of a glucoside nature, the other a slower-acting poison which appears to be an acid constituent of the resin, both, however, independent of any oil.

Many of the cases of dermatitis venenata reported in recent years have been ascribed to anaphylaxis until almost every unusually severe skin and systemic reaction that occurs during the administration or application of a drug is cited as an instance of this disturbance. The frequently seen skin reactions to quinine, iodine, iodoform, mercury and salvarsan have been cited by some as examples of the reaction. One is irresistibly struck by the clinical similarity of these reactions to the mucous membrane and skin hypersensitiveness seen in hay fever and tuberculosis, both of which are supposed to be examples of anaphylaxis. In the cases of susceptibility of certain individuals to primrose poison we are also dealing with cases of hypersensitiveness which certainly more closely coincide with our conceptions of true anaphylaxis than many of the reactions cited above. The plant at least contains a protein-like substance which in this respect, unlike iodine, mercury, salvarsan and other chemicals, fulfils one of the rudimentary requirements for a true specific anaphylaxis.

It has been demonstrated, however, that the skin irritability is not due to protein sensitization; therefore the reaction which may superficially resemble an anaphylactic reaction in reality has no direct relation to it.

In other words, we have gone far astray in our efforts to explain drug hypersensitiveness, and in our haste have distorted the theory of the reaction of anaphylaxis in an effort to make it explain a totally different phenomenon. Similar confusion resulted before the terms contagion and infection were better understood and more clearly defined.

It seems timely, therefore, to sound a word of warning against this "misnomenclature" and to recall to mind that, although anaphylaxis is not entirely understood, nevertheless there are certain fundamental requisites necessary in order to produce a true reaction.

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Richet was one of the first to suggest that anaphylaxis depended on the previous injection into or the presence in the body of some sensitizing substance or antigen. Another demonstrated fact is that such an exciting antigenic substance must necessarily be of a protein nature.

Zinsser states that the analogy between cases of drug hypersensitiveness and the phenomenon we classify as anaphylaxis is a striking one, but he agrees with Friedman that they depend on quite different processes. For instance, in drug hypersensitiveness, increased and continued administration or application of the drug increases the reaction, while in true anaphylaxis the reaction, if not leading to sudden death, decreases and finally ceases with continued administration of the antigen. Also, in drug sensitization we are dealing with a primary poison against which, in the reacting animal, a neutralizing substance is formed, a condition quite different from that seen in hypersusceptibility against primarily harmless proteins. Zinsser further states that in true anaphylaxis not only are specific antibodies present in the blood, but the production of passive anaphylaxis in animals shows that this antibody, if originating and residing in the fixed cells of the body, must necessarily also circulate in the blood stream.

In primrose dermatitis, although an example of hypersensitiveness to drugs and chemicals, the requisites of anaphylaxis are not fulfilled; and while superficially similar, the confounding of the two quite different processes is incorrect. Simpson has shown, in primrose dermatitis, that it is not possible to sensitize an animal either actively or passively with the poison of the plant, that no specific amboceptors are present in the blood of susceptible patients, that the protein of the plant has nothing to do with the reaction, and that, this being the case, it is as impossible to produce an antitoxin to the poison of the plant as it is to produce a condition of artificial specific sensitization.

Horse Serum in Pellagra. In the summer of 1916, Herold[4] had a case of pellagra of long duration which, for the first time, showed very troublesome symptoms, resembling an acute case, with the addition of the evi-

(4) New Orleans Med. and Surg. Jour., October, 1917.

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dences of postero-lateral sclerosis of the cord. The patient, a woman, would not or could not eat the right food; arsensicals had been thoroughly tried and found wanting; she was getting weaker, and delirium had set in. He realized that he had to supply her quickly with something that she lacked and which past experience, as well as the teachings of Goldberger and others, had convinced him must be in certain foods. It occurred to him that, whether this be so-called vitamins of Funk or simply albumens or nitrogenous substances, it must be in unheated blood serum; and why could not the good results obtained in transfusion be due simply to this substances transferred? Furthermore, it is known from the investigations of Dyer, Bass and others, that the coagulability of the blood is lowered in pellagra; hence, blood serum certainly would not be contraindicated, and might do much good along this line. He decided, therefore, to administer normal horse serum intravenously. After two treatments, the improvement was so marked that he gave her a third dose—all at two-day intervals. The patient improved in every way except for the central nervous lesion, and although this patient eventually died, her death being due, in part at least, to the failure of the family to follow dietary instructions, nevertheless, the temporary improvement was so marked that the method was given a further trial. Since then Herold has used it on four cases.

Herold claims for this treatment that it does in a few days what proper feeding takes weeks to do, and that it will tide over and markedly improve patients of that very troublesome class whose mouths are in such condition that feeding is almost, if not quite, impossible. The routine treatment now consists of the intravenous injection of horse serum chemically preserved, ready for use, supplemented with a lime salt, which not only aids in increasing the coagulability of the blood, but also tends to keep down the anaphylactic phenomena.

Etiologic Factors of Acne Vulgaris. An experimental study of acne and a review of the literature on the subject by Strickler[5] brought forth a number of interesting facts, but, unfortunately, there remains much

(5) Amer. Jour. Med. Sci., October, 1917.

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work to be done before the etiology of this troublesome dermatosis will be determined.

Acne is a complex disease having as a primary exciting agent the acne bacillus, to which is added the combined action of many contributing factors. This organism is probably normally present on the skin of individuals not subject to acne, but in those individuals who develop the disease the acne bacillus is activated by other factors. The activating factors are in a certain percentage of cases either the colon bacillus or its toxins, or both, as shown by the complement-fixation test and in a lesser degree by the staphylococcus or by both bacteria acting in conjunction.

To substantiate the rôle of the colon organism in acne, indol experiments were carried out, which seemed to indicate some variation in the behavior of the colon organisms from that of the normal controls. These indol experiments were, of course, only suggestive. It is probable that there are cases of acne due either to internal administration of certain remedies or to certain local applications.

In a certain percentage of acne patients there was noted an increase in the size of the thyroid gland. The exact significance of this fact can not be definitely stated. Some writers are of the belief that an increase in the size of this gland is an indication of intestinal toxemia. The use of cosmetics appears to play a rôle in the increase of this affection. There was no evidence of any relation between food anaphylaxis and acne vulgaris. Among other factors, puberty plays an important, predisposing rôle. Other predisposing factors, such as seborrhea, anemia, derangement of the stomach, nervousness, and pelvic disease, play a rôle of greater or lesser importance.

Intravenous Injection of Sodium Gynocardate in Leprosy. In a paper Rogers,[5] of Calcutta, recorded a long experience of gynocardates by the mouth, and six months' use of solutions injected subcutaneously in the treatment of leprosy, and stated that this line of treatment had given greater improvement in his hands than any other. In that paper he regarded

(5) Brit. Med. Jour., Oct. 21, 1916.

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gynocardic acid and chaulmoogric acid as synonymous on the authority of the following statement in the last (1915) edition of Martindale and Westcott's *Extra Pharmacopoeia:*

"Chaulmoogra oil contains a quantity of palmitic acid, with three other fatty acids; of these the so-called gynocardic acid (chaulmoogric acid) is supposed to be the active ingredient."

Rogers now believes that this view is erroneous, as the work of Moss, and subsequently of Power and Gornall, showed that, on fractionating the total fatty acids of chaulmoogra oil, those with the higher melting points, including palmitic and chaulmoogric acids, the sodium salts of which are very sparingly soluble in water, first separate, while Moss gave the name of gynocardic acid to the residual acids with low melting point of about 29° C., the sodium salts of which are freely soluble in water. According to Power and Gornall, Moss' gynocardic acid is not an individual substance, but is comprised of a number of fatty acids with different melting points.

What Rogers has used, therefore, for hypodermic injection in leprosy are the soluble soaps and lower melting point fatty acids of chaulmoogra oil, which, following Moss, are rightly designated gynocardic acid, and which give the characteristic reddish-brown color, changing to olive green, with strong sulphuric acid. By further fractionization, several acids with different melting points can be separated, which may conveniently be called fractions B. and C.

Rogers has found that the sodium salts of the lower melting point fatty acids can be safely given intravenously in animals in relatively large doses, and he has already used them intravenously in about twenty well-marked leprosy cases, with results which clearly show the intravenous route to present important advantages over the subcutaneous one.

Sodium gynocardates may be prepared either from the cold-drawn chaulmoogra oil, or from the buttery substance obtained by further compression of the seed of *Taraktogenos kurzii* (products of which alone are dealt with in this paper, although hydnocarpus oils are

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also being investigated, but the soluble sodium soaps of which have been found to be more irritating when injected subcutaneously than those of *Taraktogenos kurzii*) with the aid of heat obtained by steam circulating around the compression chamber. Hitherto this product has been regarded as a waste product, although it contains a large proportion of the active substances of the oil. Briefly, the method of preparation is to saponify the oil or butter with caustic potash and absolute alcohol, the soaps thus obtained being converted into fatty acids by means of sulphuric acid. These fatty acids are dissolved in hot alcohol and separated into fractions with varying melting points by gradual cooling and removal of the acids, which solidify at differing degrees. The fractions thus obtained may be further purified by dissolving in ether and recovering again by evaporating off the solvent, by which means they are rendered somewhat less irritating when the sodium salts are injected subcutaneously, for which purpose they must be neutralized accurately with the acid of phenolphthalein. When about two-thirds of the fatty acids have thus been separated the residual third, which is liquid at room temperature in Calcutta (about 28° C.), is obtained by distilling off the alcohol, and may be provisionally termed gynocardic acid C. Of the first separated two-thirds those with the higher melting points of from 43° to 40.8° C. form sodium soaps which are insoluble, or only slightly soluble, in water, and may be termed fraction A. They include palmitic and chaulmoogric acids, and are unsuited for either hypodermic or intravenous use, while it is very doubtful if they be of any value internally. They constitute about half of the total fatty acids. The remaining acids of this two-thirds have melting points from 37° to 40° C. and form sodium soaps which are freely soluble in water and may be termed gynocardic acid B. A still larger number of fractions may be separated out if desired. The best product for clinical use yet obtained was got by extracting finely divided and dried Taraktogenos seeds with ether and subsequent fractionating as above. The sodium soaps of fractions B and C mixed together caused very little local irritation when injected subcu-

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taneously, while the observations on intravenous injections recorded in this paper are mainly based on the use of this product, which clearly contains all the lower melting point acids of both the cold compressed oil and the butter obtained by further compression of the seeds with heat. It is referred to as fractions B and C of the whole seed.

For intravenous injection of sodium gynocardates a 2 or 3 per cent. solution may be made in distilled water (or normal saline), and after sterilization in an autoclave 0.5 per cent. phenol is added. For intravenous use the solution should be quite clear, and if any precipitate forms it should be filtered and resterilized.

The two great advantages of the intravenous over the subcutaneous method are its painlessness and greater efficiency. As nearly all the author's cases are Indian out-patients, over whom there is no control, some of them ceased to attend long before any material result could be expected from the subcutaneous injection, on account of the pain and induration at the seat of injection. Since the intravenous route has been used no such disappointments have been experienced. Of much greater importance is the more rapid improvement which has been observed to follow the intravenous injections, which is already clearly evident. Several months are required to produce any decided improvement by the subcutaneous method, whereas, especially in tubercular cases, the progress is apt to be disappointingly slow even after it has started. It is far too early to say what will be the ultimate results of the intravenous medication, but present experience is decidedly encouraging.

The most striking result of the intravenous infections is the occurrence of definite local reactions in the diseased tissues, sometimes accompanied by fever, which has been seen in several cases after from 2/5 to 3/5 grain of sodium gynocardate intravenously, of a degree that has not been seen to occur after subcutaneous injections. The most decided reaction was in the greatly thickened ears in a tubercular case; fever occurred for three days with redness and swelling of the helix, accompanied by some serous discharge containing broken-down leprosy bacilli. After the subsidence of the reaction at the end

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of ten days the diseased tissues were decidedly softer and less indurated than before, while nodules on the face, not showing the local reaction, were also diminished in size. In another patient with very large tubercles on the face, a similar but less acute reaction was also followed by distinct improvement. In two anesthetic cases, with greatly thickened ulnar nerves, tenderness and slight swelling appeared in the affected portions after intravenous injections, which has been followed by some return of sensation in previously anesthetic areas of the hand. One of these patients also had fever, but previously had been subject to it. It is thus clear that intravenous injections of the drug have produced selective local reactions in the diseased tissues, which have been most evident in those patients with the greatest amount of infiltration of the tissues with leprosy bacilli, so they are most interesting and suggestive. It is too early to say whether the drug should be pushed to the extent of producing such reactions, but Rogers is inclined at present to think they are decidedly beneficial when moderate in degree, although the possibility of dissemination of the bacilli in the body must not be lost sight of.

Rogers has now given about two hundred intravenous injections of gynocardate, and his experience has led him to substitute the intravenous almost entirely for the subcutaneous method. Further experience is required to ascertain how far it is advisable to push the dosage, but there can be little room for doubt that even half a grain intravenously is likely to have a greater effect than four grains slowly absorbed from a subcutaneous injection. The intravenous method is likely to prove as great an advance on the subcutaneous one as the latter has on the oral administration of gynocardates or chaulmoogra oil.

A New Ulcerative Dermato-Mycosis. Castellani[6] describes a peculiar ulcerative disorder which is clinically characteristic, and which is rather common in Ceylon. Recently he has observed a case of the same disease in the Balkans. It is of hyphomycetic origin, as was found

(6) Brit. Med. Jour., Oct. 7, 1916.

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by the fact that the same fungus was grown from all the cases.

As a rule no hyphomycetic elements are seen microscopically in scrapings from the ulcers and contents of the nodules. If, however, the material be inoculated in glucose-agar tubes, small, yellowish, amber-colored colonies appear from four to eight days after inoculation; they enlarge rather rapidly; become hemispheric, and often coalesce in a knotty mass. At times the colonies may not fuse together; each colony then remains separate, reaches a large size, and occasionally presents peculiar radiating furrows, as seen in certain species of trichophytons. In many cases, when the material has been collected from ulcerated lesions, the fungus grows in symbiosis with a coccus, and it may be somewhat difficult to separate the two organisms. When the inoculations have been made from lesions not yet ulcerated, the fungus only is present. The disease has been easily reproduced in two coolies (who volunteered) by injecting cultures of the isolated fungus. Cultures used for such experiments must be recent, as old cultures apparently lose their pathogenicity. The experiments on this subject will be reported in detail later.

Professor Pinoy of the Pasteur Institute investigated the fungus and found it to belong to the hyphomycetes or *Fungi imperfecti.* He proposes to include it in the genus *Accladium,* at least temporarily, and to call it *Accladium castellanii.*

The microscopic appearance on culture media (Sabouraud's agar, carrot) recalls somewhat the appearance of *Cladosporium herbarium,* with the difference that the colonies are whitish and amber yellow instead of being greenish-black. The growth consists of many small roundish masses which later on often coalesce, covered by spiculated formations consisting of erect, straight filaments parallel to each other or at times interlacing.

In a well-marked case ulcers are seen practically all over the body, though on the face, scalp, palms and soles they are in small numbers or altogether absent. The ulcers are generally sharply defined, roundish, or oval, with red granulating fundus. Their appearance is

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PLATE II.

Microscopic appearance of *accladium castellanii*. (A) 1 day; (B) 3 days, and (C) 5 days old.

Artificial culture of *accladium castellanii*.

Mycotic lesions on the forearm.—Castellani (see page 19).

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well shown by the photograph of the arm reproduced in Plate II. In certain cases there may be abundant purulent secretion, and the ulcers are often covered by thick yellow crusts. Gummata-like nodules and furuncle-like lesions may also be observed. Some of the superficial lymphatic glands are often enlarged. The lesions are not, as a rule, very painful and there is little or no itching. The general condition of the patient is not seriously affected for a long time, but he often complains of weakness, general discomfort, and is unfit to attend to his work. Occasionally there is serotine temperature. In two cases in which the blood was investigated red blood corpuscles and hemoglobin were slightly below the normal, and in one case there was eosinophilia (5 per cent.). This feature of the blood may, however, have been due to intestinal parasites, as the stools contained eggs of ascaris. The urine did not contain either albumin or sugar.

The course of the disease is long, and if left untreated there is apparently not much tendency to spontaneous cure.

Most of the patients came with the diagnosis of syphilis, but in only one was there a history pointing to that infection, and in two of the cases in which a Wassermann test was carried out the result was negative. Moreover, scrapings from the ulcers never showed spirochetes, and salvarsan and mercury have no beneficial effect of the condition.

As already stated, the course of the disease is very long, and there is little tendency to spontaneous cure; on the other hand, if properly treated, a complete cure can be obtained rather rapidly.

Potassium iodide acts fairly well. It should be given in full doses, gr. 20, three or four times daily. The drug appears to act better if the patient be given a salt-free diet, as first suggested by Professor Pinoy in other dermatomycoses. Mercury and arsenic have no beneficial effect on the course of the malady. As regards local treatment, it is sufficint to keep the ulcers clean by dressing them with weak mercury bichloride lotion. Ointments are badly borne in most cases.

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Trade Dermatitis.

Industrial Eczema. The work of Apfelbach,[7] Medical Director, Division of Factory Inspection, Illinois Department of Labor, deals chiefly with the diagnosis of lead and arsenic poisoning among employees of factories and trades using the above and other occupational poisons. The fact, however, that so many workers seek medical advice for skin lesions in an occupational disease dispensary prompts this writing, more from the industrial hygienist's standpoint than from an accurate knowledge of dermatology.

Certain skin lesions, as, for instance, chrome ulcers and aniline dermatitis, are peculiar to the occupation, with no question of doubt as to their occupational origin. Most of the skin lesions entering the dispensary are determined as occupational by the following requirements: (1) That the lesions improve when the sufferers leave their occupation; (2) that no trouble existed before entering the suspected trade; (3) that there is present one or more of the recognized skin irritants or the suspicion of such (for investigation).

Occupation is not always the direct cause of dermatitis, but often only predisposes certain individuals to skin lesions. It is granted that certain skins are invaded more easily by bacteria and other parasites. The industrial hygienist disregards whether lesions occurring in an occupation are predisposed thereby or actually produced, and concerns himself more with the recognition of the conditions and their prophylaxis.

The skin may be injured or may become diseased in occupations in different ways, such as through the effect of heat, cold, mechanical irritation, trauma, acids, alkalies, metals, plants and even animal irritants.

If any occupation has a hazard for skin disease some workers will and some will not become affected. Besides the causative agency there must usually be an idiosyncrasy or tendency for that person to suffer skin disease. The severity of the lesions of the skin depends on the resistance of the individuals against secondary invasion by pathogenic bacteria.

(7) Med. and Surg., September, 1917.

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Some skin lesions from occupation are mild and merely of interest, as, for instance, the sunburn of the farmer, the heat dermatitis of stokers and furnace men, and callus of the zither and violin player, and the lip dermatitis of the flutist. In others the lesions are more serious, as, for instance, arsenical ulcers, chrome ulcers, and the anthrax pustule of the tanner and wood sorter.

The following points should be kept in mind concerning industrial skin diseases:[8]

1. Among any group exposed to skin irritants, some will acquire a tolerance for the irritating agents, others will suffer.

2. Sometimes an irritating agent will continue for a long period of time before skin lesions appear.

3. In addition to the irritating agent there are always on the skin pathogenic bacteria, which may complicate a simple dermatitis with pus infection.

4. Most skin lesions due to occupation begin on the hands (arsenic on the scrotum). Trousers or underwear may, however, allow exposure, so that lesions are also found on the legs.

Tuberculosis.

Acnitis in the Negro. The titles used as descriptive of the disease show that the field is divided as to whether acnitis should be classed under those conditions related to tuberculosis of the skin, or should be viewed as a distinct entity. Investigations which would prove conclusively that the disease was related to tuberculosis cutis have been, in most instances, negative. Knowles[9] reports an interesting case occurring in a negro who was 26 years old and who had had the lesion limited to the face and neck for six months. The lesions were papules or nodules, were very numerous, and varied in size from a pin head to a split pea. The patient had symptoms and physical findings suggestive of pulmonary tuberculosis but no bacillus was found in the sputum. The von Pirquet test was positive.

(8) A short list of occupations showing toxic agents and also a chart listing some of the more toxic agents, appear in Practical Medicine Series, 1917, Vol. VIII, pp. 343-345.

(9) Jour. Cut. Dis., February, 1917.

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Histologically, the epidermis was found practically normal, excepting for the lengthening of a few rete pegs, and for the fact that the growth had broken through one small portion of this layer.

The corium showed a considerable number of cell masses, particularly prominent in the middle and subpapillary portions of this layer. These cellular infiltrations were of a rounded and longitudinal formation, varying considerably in size. They consisted of three distinct types of cells; small round cells, resembling those seen in ordinary inflammation; epithelioid cells; and large multinucleated cells, apparently giant cells. The cell masses were arranged in distinct groups, with usually a well-defined border. The corium between some of these cell infiltrations appeared normal. These groups of cells consisted of from a dozen or more, up to hundreds. There was a distinct tendency for the central portion of the cell infiltration to exhibit numerous giant cells, with epithelioid cells interspersed and surrounding the same, and a large number of small round cells forming the circumference. Although this was the dominating tendency of the growth, in some sections the major portion of the infiltration consisted of giant cells, in others epithelioid cells, while in still others there were almost exclusively small round cells. There was an increase of fibroblasts, surrounding some of these cell areas. Plasma cells were absent and mast cells were present in normal numbers.

Giant cells were numerous, mostly in groups; as many as twenty or thirty were seen in a single field. They were mostly of a rounded conformation, although some were oval or elongated. From a half dozen to twenty nuclei were observed in each cell, and they were arranged mostly around the entire circumference; but in others there was a segmental distribution. Occasionally a giant cell was seen, in which nuclei were also present in the central portion, as well as peripherally. A few giant cells were observed entirely alone in the corium, without the usual accompanying epithelioid and round cells. The giant cells varied tremendously in size, some being almost double the dimension of others. Very few of

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these cells conformed to the Langerhans type, but were probably of thrombosed blood-vessel origin.

The growths were well supplied with blood-vessels, both peripherally and running into the cellular infiltration. This central supplying of blood to the cell masses was, however, observed only in the beginning lesions. In the older lesion there was a distinct tendency toward coagulative necrosis in the center of the growth. Some of the growths could be distinctly seen to lie in the course of the small blood-vessels; two or more vascular branches from these channels were plainly visible, running into these infiltrations. The blood-vessels were widely dilated, and quite a number of them were surrounded by small round cells, in some instances apparently continuous with the growth into which they ran. The endothelial linings of the vessels were quite swollen. Some of the sections showed considerable edema of the tissues and widening of the lymph spaces and channels.

The hair follicles and the sebaceous glands were closely surrounded by some of the growths, but showed little involvement. The sweat glands also, excepting for a slight infiltration with round cells, in some instances, were practically normal.

Pustulation in one of the excised lesions gave rise to a mass of leukocytes which presented a typical picture of an acute inflammatory process.

There is a great diversity of opinion as to the derivation of the pathologic process observed in acnitis. Pollitzer considers that the affection is of sweat-gland origin and that both the giant cells and the nests of epithelioid cells are derived from these glands. Pernet also believes that the fault lies in the sweat glands. Barthelmy is of the opinion that the process begins at the base of the hair follicle. Schamberg, Spiegler, and Finger found the diseased process in close proximity to both the hair follicles and the sweat glands. Jesionek found the cellular infiltration surrounding the hair follicles, sweat and sebaceous glands, although suggesting that it might have had its origin in the blood-vessels surrounding these organs. Ketron apparently has traced

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the origin of the growths, in his case, from the small vascular channels which run into the growth.

The sections examined by this author in the present case are very suggestive of blood-vessel origin, as found by Ketron, notwithstanding that the cellular infiltration is found, in some instances, in close proximity to or actually involving, the hair follicle, sebaceous and sweat glands. It has been extremely interesting to compare sections from so-called sarcoid and lupus vulgaris, with the present case; and the resemblance between the three is very marked, notwithstanding that the consensus of opinion points toward the inflammatory nature of acnitis and that there are very few giant cells of the typical Langerhans type present, but mostly those conforming to the thrombosed vessel variety.

Four months after the writer's patient came under observation, all the active lesions had disappeared. Some had undergone involution without the production of scars but the majority left round, oval or irregularly shaped, pit-like cicatrices. The mild applications and *x*-ray treatment employed, apparently had little effect upon altering the course of the affection.

This is the first case of acnitis that has been reported as occurring in the negro, in so far as Knowles has been able to ascertain.

Lupus Pernio and Sarcoids. A study of three cases leads Schaumann[1] to conclude that lupus pernio and cutaneous sarcoids are symptoms of one and the same disorder. This disease is a tuberculoid lymphadenitis which is characterized by the multiplicity of its lymphatic localizations in the ganglia, tonsils, bone-marrow, lungs, kidney and liver.

In common with other types of lymphadenitis this disorder presents cutaneous manifestations of two kinds: The one, of the same nature as the internal lesions, are those described under the terms of lupus pernió and cutaneous sarcoid; the other manifests itself as a common prurigo. The latter has no relation to tuberculosis, nor to any other known infection; it is an infectious granuloma running a benign course and should be called a benign lymphogranuloma.

(1) Ann. derm. et syph., 1917, p. 357.

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Mycosis Fungoides.

Localized Mycosis Fungoides. The second case of localized mycosis fungoides seen within the past year at the University of Michigan is reported by J. A. Elliott.[2]

Over the upper third of the forearm there was an irregular ulcer from four to five inches in its long axis and two inches across, the long axis being across the arm. The edges were irregular, slightly raised and erythematous with a slight sero-mucous exudate, the base of which was covered by a thin black crust. Over the elbow, there was a much larger irregular ulceration, extending about half way around the arm and about six or seven inches in diameter. The base of this lesion was necrotic with marked loss of tissue at its center, forming a crater-like lesion. The tissue immediately surrounding these ulcerations was slightly erythematous, infiltrated, and in places covered by a slight scale. On the under side of the elbow there was a small ulcer the size of a quarter with a rolled border and a clean base, which had a serosanguinous discharge. Just above the large ulcer on the outer aspect of the arm there was an irregular, raised lesion which was composed of small confluent nodules of a purplish color and covered by a slight scale. In the center of these lesions there was a depression which consisted of blanched out tissue resembling a scar, the site of an involuted lesion. On the upper portion of the arm over the outer axillary fold was a large circular lesion, raised about an eighth of an inch above the normal skin. It had a nodular appearance and was covered by a slight scale. Throughout the lesion there were small points of necrosis. The skin extending from the lesion under the arm was red, infiltrated and was also covered by a slight scale. Its extent was, however, very definitely demarcated. The edema of the entire arm was very marked, but more pronounced over the back of the hand and forearm. The glands in the axilla were markedly enlarged.

The general examination was negative. The blood showed 34 per cent. eosinophils on entrance. The leu-

(2) Jour. Mich. State Med. Soc., March, 1917.

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kocytes had been as high as 30,000. The patient received *x*-ray therapy with iodides and the lesions decreased very much in size. The large lesion on the back of the arm healed rapidly.

Leprosy.

Leprosy in Connecticut. Leprosy is very rarely seen in this part of the United States, and only one case has been seen in Connecticut in recent years. It is for this reason that the following case is briefly reported by J. E. Lane.[3]

On Nov. 20, 1916, T., aged 20, presented himself at the dermatologic clinic of Yale University, showing the usual features of a well-developed, though not severe, case of the nodular type of leprosy. There were nodules, dirty brownish gray pigmentation, areas of anesthesia, analgesia, and hyperalgesia, general glandular enlargement, and thickening of some of the nerve trunks.

The Wassermann reaction, as is usual in these cases, was strongly positive. Leprosy bacilli were easily demonstrated in smears of the nasal secretion. Secretions of an excised nodule were filled with masses of the bacilli.

The chief interest in this case is the fact that leprosy patients wander about for a long time without being recognized, as a majority of the physicians have never seen a case of the disease, and quite naturally do not suspect it.

This patient was living in a nearby town, where he had been for six weeks. He was a Greek, born in Thessaly, and he came to New York in 1912. Since that time he has lived in different places in New York, in Pennsylvania, in West Virginia, and in three or four towns in Connecticut.

Tropical Diseases.

Barcoo Rot. By the middle of the summer of 1916 a number of men of the Anzac mounted division, which

(3) New York Med. Jour., Dec. 23, 1916.

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had been operating in the desert east of the Suez Canal for over six months, suffered from spreading superficial ulcers on the back of the hands, extensor surface of the forearms and, to a less extent, on the back of the feet and on the shins. The ulceration, Lieut.-Colonel C. J. Martin[4] says, resembles that met with in bushmen in the back-blocks of Australia, and is known locally as barcoo rot. It was recognized by the men as the same disease they had seen or experienced in Australia.

Superficial ulcers were also troublesome during the Boer war. They affected troops kept on trek on the high veld, and the disease was labelled "veld sore." Troops apparently are not liable to veld sore until they have been at least three months in the country. Life during the dry weather in the Australian back-blocks, and campaigning on the high veld, or the Sinai desert, present conditions which are not unlike. In all three cases, water for washing is minimal; prolonged subsistence upon bread, biscuit, and salt or tinned meat, with lack of fresh vegetables, is the rule. Furthermore, appropriate dressing of the sores in the early stages is difficult or impossible while the patient continues his occupation. Like veld sore, barcoo rot is difficult to cure in the above conditions, but readily yields to treatment when the patient comes into one of the towns. To what extent this is to be attributed to facilities for greater cleanliness, appropriate surgical dressing, or to dietetic improvements, is uncertain.

The patient may remember abrading the skin, but whether or not, the first sign is usually a bleb or blister containing thin watery pus and surrounded by an area of slightly inflamed skin. The blister may be the size of a sixpence (a little larger than a dime), or even larger, but before it reaches this size it is generally broken. The denuded surface shows little tendency to heal, but slowly extends at its margins, at the same time deepening until there are no more epithelial structures left. The ulcer, however, remains shallow, and it is unusual for the fibrous layer of the skin to be destroyed unless it becomes infected with virulent staphylococci.

(4) Brit. Med. Jour., June 9, 1917.

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The glands are not inflamed unless secondary infection occurs, and there are no constitutional symptoms.

When healing has occurred areas of glossy skin, more or less denuded of hairs and sweat glands, are left. Cicatrization does not occur unless the true skin be destroyed. Infection of fresh areas of skin in the neighborhood is usual, so that the patient has several ulcers of different ages. The disease in its minor forms is extremely annoying and, when the ulcers have become large, incapacitating.

The symptoms and pathologic findings have no resemblance to the slowly evolving leishmaniasis known under the names of *Bouton du Nil, Clou de Biskra and Bouton du Caire.*

On a visit to an outlying field ambulance, the author saw twenty men admitted for obstinate ulcers of considerable extent. The ulcers were shallow, mostly on the back of the hands and wrists—that is, in areas exposed to small injuries, and rich in hairs. The smooth surfaces were free from ulcers, and the progress of an ulcer appeared to be inhibited as soon as it extended to a hairless portion of skin.

It seemed advisable to examine the state of the hair follicles, both within and around the ulcers, and a number were epilated both from the base of the ulcer and from the reddened slightly swollen skin at the margin; many of the hairs were loose.

Infection of the hair follicles was confirmed by microscopic examination of fresh material, and cultures from the bases of removed hairs and from the contents of early blebs were made upon blood agar and ordinary agar. *Staphylococcus albus* was the predominating organism, but some *S. citreus* and a few *S. aureus* were also present. In one case a diptheroid was abundant. This proved to be *B. diphtheriae.*

The microbial infection of the hair follicles appeared to be confined to the connective tissue sheaths, except in very badly affected hairs, in which the base was disorganized and the layers of the root sheaths unrecognizable.

The pus from the early blisters before they were broken afforded only growths of staphylococci. Gen-

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erally, there was a hair, often a very small one, passing through them, and the follicle of the hair was invariably infected with staphylococci.

Martin's observations on the bacteriology of barcoo rot are in general accord with those of Ogston (1901) and Harman (1904) upon veld sore. Ogston and Harman, however, make no mention of any infection of the hair follicles. Ogston saw only Gram-positive cocci in fluid from the edge of ulcers. Harman cultivated only staphylococci from the unbroken vesicles. These gave the cultural characters of *Staphylococcus pyogenes aureus*, but grew rather more abundantly on culture media than a virulent strain with which they were compared. They were not virulent for rabbits. Harman was much impressed by the resistance to heat, to the effects of drying, and to the action of corrosive sublimate possessed by his cultures, but this was probably not greater than has been met with in some strains of staphylococci.

The epidemiology of veld sore was carefully studied by Harman, but he could find no indication that the infection spread from one to another among the troops, and barcoo rot affects men living in solitude. Neither disease seems to be associated with particular occupations. It would seem probable that barcoo rot, and possibly veld sore too, is due to the infection of the epidermal structures with staphylococci of low virulence, such as abound upon the skin. In barcoo rot the infection of hair follicles is apparently the common way in which it begins, and the usual manner in which it spreads at the margin of the ulcer.

In hospital, the ulcers generally heal up slowly under any sort of wet antiseptic dressing, but are very difficult to deal with in the field. A wet dressing is unhandy when a man has to go about his business and it is difficult or impossible to change it frequently enough. Moreover, in a hot climate it soon becomes converted into a dry dressing and adheres to the ulcer.

In view of the observations on the pathology of barcoo rot described above, it seemed not unlikely that the infection of the hair follicles was largely responsible for the continuance of the ulcerative process in the

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center, and its progress at the margins of the ulcer. Careful epilation of all the infected hairs and of the normal hairs for some distance beyond the margin of the lesion led to prompt healing and stopped the extension of the infection.

Tegumentary Leishmaniasis in Brazil. Rabello[4] reviews the history of oriental sore in Brazil and describes the clinical manifestations and the treatment of the disease in that country.

The first description was made by Adeodito in 1895 but the first intensive studies were made by Luidemberg, Carini, Paranhon, and the author during the epidemic in Bahurn in 1905. In 1906 Shlendone reported lesions of the mucous membranes in addition to those of the integument. Both may be found in the same patient.

The cutaneous lesions may be (1) nodular, (2) papillomatous or vegetating, or (3) ulcerated. The latter form is the one most commonly encountered. It begins as an itching furuncle with a red areola on the exposed portions of the body, and rapidly develops into an ulcer. The lesions vary widely in size, have regular outlines and a granulating floor. Scratching may result in the development of new lesions by autoinoculation. Not infrequently, lesions are seen healing by cicatrization on one margin while advancing on the other. The ulcer may persist for months or even for three years without spontaneous healing.

The non-ulcerating forms seen in Egypt and India apparently do not exist in Brazil. The papillomatous or verrucous lesions, however, are quite common, and usually occur about the muco-cutaneous junction of the nose and mouth.

The ulcer of the mucous membrane usually begins in the outside of the nose. In time this may spread to the pharynx, mouth and tongue. Extensive verrucous lesions, or marked destruction of the soft parts of the nose may occur with seemingly little disturbance of the general health.

The disease occurs most frequently among the rail-

(4) Bull. Soc. derm. et syph., July 14; Dec. 15, 1915.

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road laborers of northern Brazil. Age and sex seem to be of no etiologic significance.

Morphologically, the organism is the same as that of *Leishmania furunculosa* but clinically the lesions are much more formidable than oriental sore. The intermediate host is thought to be an insect.

The differential diagnosis clinically is exceedingly difficult. The lesions may closely stimulate tuberculosis, syphilis or lepra. The lesions about the nose resemble lupus vulgaris. Those of the palate are very much like syphilis and, moreover, the Wassermann reaction may be positive in the absence of the latter disease. The only method by which a positive diagnosis can be made is by microscopic examination of scrapings or of sections for the parasites.

The best treatment is the intravenous injections of 1 per cent. solution of antimony and potassium tartrate in normal saline, which should be rendered sterile by passing through a Chamberland filter. The injections are given two or three times weekly and after six or seven injections the cutaneous lesion heals by cicatrization. The mucous lesions are much more resistant to treatment and it is sometimes necessary to repeat the injections for several months.

Granuloma Venereum. Granuloma venereum, synonymous with granuloma of the pudenda, groin ulceration and serpiginous ulceration of the genitals, was first discovered in India (1882) and afterward in many other tropical or subtropical countries. Occasionally a case is seen in Europe or North America in people who have never lived in warm countries.

Granuloma exists, according to Aragao,[5] on the east coast of South America from the Guayanas to the Argentine Republic. In Brazil, for a long time the cases were not recognized, and were generally confounded with venereal or other diseases until, in 1909, F. Terra, professor of dermatology in Rio de Janeiro, published the first case, with the diagnosis of granuloma. Rabello, in 1912, found Donovan bodies in smears of the same case. In the same year, together with the late Gasper Vianna, Aragao studied several cases of granuloma,

(5) New Orleans Med. and Surg. Jour., October, 1917.

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demonstrating the microbe first seen by Donovan, and studied its nature. He also discovered a new and very effective treatment by means of intravenous injection of tartar emetic.

The clinical forms of granuloma observed in Brazil are similar to those described from other countries and appear as torpid serpiginous ulcers, situated on and around the genitalis and which last many years without tendency to spontaneous healing. A localization in the mouth is rare, but this has been seen in Brazil.

Views on the etiology of granuloma have varied widely. On the one side it has been considered as a manifestation either of tuberculosis, syphilis, framboesia or leishmaniasis, whereas on the other, it has been attributed to a specific agent, a bacterium, a treponema, or a fungus. Of all these microbes, only one is constantly present, and by its general qualities may justly be considered as the cause of the disease. It was first found in 1905 by Donovan, and became known under the name of Donovan's bodies; later on it was well described by Siebert and Flu, who considered it belonging to the bacteria with capsules. In Brazil this microbe has been found in all cases of granuloma. Aragao has given it the name of *Kalymmato bacterium granulomatis*. It does not take the Gram stain and is only weakly stained by the common aniline dyes. Its characteristics appear well only with Geimsa's stain, which shows the surrounding capsule very distinctly. This capsule contains small, round or ovoid bodies in the shape of small cocci of about three-tenths of a micron, which afterward stretch and appear as small rods from one-half to one micron in size. On dividing, they show a dumb-bell form, and the constriction increases till a complete separation occurs. The germ then appears under the form of a diplococcus; the elongated capsule soon gets strangulated in the middle and finally the products of the complete division separate (Fig. 1, Nos. 1-5).

A special characteristic of the germ of granuloma is its localization in the tissues, where it appears principally in the protoplasm of certain cells, and, by its multiplication, assumes a very characteristic aspect

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(Fig. 1, Nos. 6 and 7). In sections, free germs are generally in smaller number than those in the interior of leukocytes and cells of the connective tissue (Fig. 1, No. 7). The plasma cells, though very abundant in granuloma tissues, never show germs in their plasma, as Flu asserted.

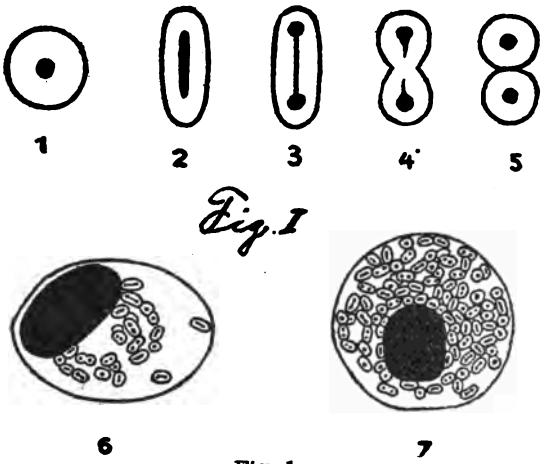

Fig. 1.

Inside of the cells the germs sometimes appear without their capsule. They form at first a zooglea of varying size near the nucleus, similar to chlamidozoa, in their appearance, as Flu pointed out (Fig. 1, Nos. 1-4). Afterwards the elements of this zooglea separate, showing now the characteristic capsules. The infected cells first become hypertrophied, the nucleus being dislocated by the germs. Later the cells become destroyed. Often also the microbe degenerates in the cells and is reduced to fragments, leaving débris which it is often impossible to identify.

The germs of the granuloma are found over the whole extension of the ulcers, but mostly in the zones where progression takes place.

In culture experiments, Aragao first obtained in three granuloma cases, by the use of Sabouraud's medium, a

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capsule bearing bacterium, very much like the bacterium of Friedlander in morphologic, cultural and pathogenic characteristics. For this reason, he had some doubts at first about its identity with the tissue germ. It grows well on all laboratory media, and when injected into guinea-pigs, rabbits or marmosets, kills them in twenty-four hours with profuse septicemia. Inoculations of laboratory animals with the tissues of granuloma failed to produce the disease.

The difficulty of curing granuloma is generally admitted. Many treatments have been tried, such as cauterization, mercury and all the various arsenical preparations, including salvarsan and neosalvarsan. Extirpation can be used only in cases without extensive involvement. Up to a certain time, the only treatment giving favorable results was the use of Roentgen rays. Having used vaccino-therapy without result, Aragao resolved to try injections of tartar emetic, which had proved so efficacious in leishmaniasis. With this treatment he obtained very good results by rapid cicatrization of the lesions of granuloma. He used tartar emetic in the same way as in leishmaniasis. Intravenous injections of from 10 to 12 c.c. of a 1 per cent. solution in sterilized physiologic salt solution are given. The injections are generally well tolerated, but occasionally the patients complain of cough and passing rheumatoid pains, which do not interfere with the treatment. The number of the injections varies according to the character of the lesions and the rapidity of cicatrization. When the lesions are healed the treatment must not be discontinued, but should be continued for another ten or twelve injections, in order to insure cure. It is advisable to give another series of twelve injections two months after the first treatment, to prevent a return of the disease, which is common when such precautions are not taken.

Blastomycosis.

Systemic Blastomycosis, with the Stomach as a Possible Port of Entry. A case of systemic blastomycosis is described by Sihler, Peppard and Cox,[6] which is the

(6) Journal-Lancet, April 15, 1917.

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first case to be reported from the state of North Dakota. The case was carefully studied both clinically and at autopsy and is peculiar in that it lacked the cutaneous and subcutaneous lesions which have been quite constant in the other reported cases, and which have led to a diagnosis. It is also the first reported case having recurrent ascites as a finding.

A stomach ulcer with the localization of the blastomycetes in the stomach wall suggests this is a portal of entry. The gastro-intestinal tract has not heretofore been seriously considered as a point of entrance.

Keratosis Blenorrhagica.

Hyperkeratotic Exanthem in Gonorrhea and Syphilis. The rarest complication of gonorrhea is the hyperkeratotic exanthem first described by Vidal and later by other French writers.

The horn formation may be present from the onset as a papular eruption, or it may be preceded by vesicular or pustular lesions. The lesions may be generalized but as a rule are limited to the palms and soles.

The eruption appears usually in one of two forms. In one form the lesions are found on the palmar and plantar surfaces as broad, flat, horny masses of a yellowish-brown color. In the other form the lesions are small, round, greyish-white, elevated, conical, and sharply circumscribed from the normal skin, or surrounded by a red areola.

Once developed, the lesions persist for a long time and resist all therapeutic measures.

Nathan[7] carefully studied a case that was particularly interesting because of the fact that the lesions appeared during the secondary manifestations of syphilis.

The patient was a man of 39, with gonorrhea and a gonococcus arthritis of the left ankle. On the body were pigmented relics of an exanthem and in the urethra was the indurated papule of an old chancre. The Wassermann reaction was negative.

About three weeks after he came under observation

(7) Archiv. f. Derm. u. Syph., 1916, Vol. 121, p. 906.

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pustular lesions appeared on the left sole, and later similar lesions developed on the right sole. The lesions were surrounded by a red area, and in the course of a week developed horny scales, and eventually hyperkeratoses.

On both feet, especially the great toes, on the dorsa, and along the inner, upper plantar margins were lentil- to small coin-sized horny excrescences which varied in height from 2 or 3 mm. to 1 cm. They were mostly in the form of blunted cones, which were occasionally crateriform. On the plantar surfaces the horny masses were more flattened and very tender. After removal of one of the keratoses it left a moist, reddened base with a bluish-red margin.

Histologically the epidermis was found to be thinned with an increase in the length of the rete pegs. The kerato-hyalin layer was absent. There was a thick layer of parakeratotic cells within which there was an infiltration of leukocytes which also involved the corium. There were also changes in the interna and media of the small vessels of the corium.

The presence of secondary manifestations of syphilis brings up the question as to whether it played any rôle in the pathogenicity of the eruption. Against this assumption is the fact that in all hitherto reported cases the lesions appeared only with gonorrhea, and recurred with repeated attacks. In favor of it is the fact that in this case salvarsan therapy caused a disappearance of the lesions.

Ringworm.

Tinea Tonsurans in an Adult. Trichophytosis capitis is exceedingly rare in the adult. An interesting case is reported by Oliver[8] of a woman whose two children were under treatment for ringworm of the scalp and who also developed a typical patch in the scalp. The patient had been using the same comb as the children for two months. Cultures showed the organism to be *M. audouinii.*

Abnormal Growth of Hair After Kerion Celsi. In

(8) Brit. Jour. Derm., Vol. 29, 1917, p. 34.

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1915 Kuznitzky[9] reported a case of alopecia areata in which the areas became covered first by lanugo hairs which were later replaced by hyperpigmented coarse hairs.

Fuchs[1] reports a similar growth of hair following kerion celsi which had been treated with mercury, sulphur and pyrogallol ointments applied to the entire scalp and generalized epilation with the roentgen ray. Locally hydrarg-gutta plaster was applied.

The lesions healed with slight scarring without recurrence. In the small scars left by the kerion occurred an hypertrichosis of coarse pigmented hairs. Later the entire scalp developed similar hairs so that the contrast in appearance disappeared.

Fuchs is unable to explain the abnormal growth of hair. Possibly the physico-chemical irritation by the plasters and ointments may account for it. Or it may have been due to trophic disturbances occurring in the scars.

Acarus Infection.

Eruption Associated with Demodex Folliculorum. The morphologic characters of the skin parasite known as *Acarus*, or *Demodex folliculorum*, are sufficiently familiar to need no detailed description. As is well-known, it was first discovered in cerumen by Henle in 1841 and as an inhabitant of human sebaceous glands by Simon in 1842, and in the monumental treatise on skin diseases published by Erasmus Wilson in 1846 a special chapter is devoted to an exhaustive notice of its anatomic structure and possible pathogenic qualities. From that day, successive generations of dermatologists have recognized its presence and discussed its significance with a fairly unanimous agreement that it might be regarded as harmless.

What is not so generally known is that almost coincidentally with Simon's discovery, Tuck described the same parasite as present on the skin of dogs, and that it is as well-known to veterinary medicine as to our own

(9) Practical Medicine Series, 1915, Volume IX, p. 121.
(1) Archiv. f. Derm. u. Syph., Vol. 121, p. 945.

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practice; but here it has a definite pathologic meaning.

The eruptions described in the dog are both squamous and pustular in type, and the latter is the more common. This form may also occur in circumscribed patches, especially on the head (nose, lips, eyelids) and the paws, but may also spread all over the body.

For some years Lawrence[2] has entertained increasing doubts as to the entirely harmless nature of *Demodex folliculorum* in human beings. At the International Dermatological Congress, held in Rome, in 1912, he exhibited a moulage of an impetiginous eruption on the face of a young adult, from which he obtained numerous specimens of demodex. The association was so marked that he considered they must have played an important part in producing the inflammatory condition of the skin.

Recently the author has seen four cases of an impetiginous eruption in adults associated with the presence of great numbers of parasites. These cases have occurred in adults, and resemble an impetigo contagiosa, but there would seem to be some difference from that affection. The lesions have a greater tendency to form rings, and the border of the skin is more definitely raised than in ordinary impetigo contagiosa. The pustulation is not so severe as in impetigo, nor do these cases respond so rapidly to the usual simple antiparasitic remedies as might be expected. Some patients have thought the eruptions followed shaving, but the lesions may be situated away from the hairy region, and be found on the forehead, neck, or on the nose.

The feature common to all these cases is the extraordinary numbers of *Demodices folliculorum* which are demonstrable in the most simple scraping from the skin. Five or more may be seen in a microscopic field, and their size varies in quite a remarkable degree, possibly representing successive generations.

Certainly it is possible to obtain an odd specimen of demodex by squeezing the sebaceous matter from the skin about the nose; but that does not seem to meet the explanation required of the great numbers found in the affection here described, and it might well be

(2) Med. Jour. Australia, December, 1916.

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that they play some active part in producing the eruption itself.

It is, of course, a parasite observable in a number of skin conditions, and is sometimes found in large numbers in cases of acne rosacea. It may, conceivably, lose its harmless character in one of two ways; either by an enormous increase in number or by its association with some pus-producing organism.

The treatment Lawrence has found most efficient is to paint the lesions with tincture of iodine, after rubbing the parts with a salicylic and boracic ether lotion.

Obviously, it would be difficult to produce incontrovertible evidence of the relation of the demodex to this affection as being that of cause and effect, since it is impossible to undertake experimental inoculation, except from man to animals, and this possibility appears to have been settled by Gruby in 1845. Points that may be considered established are: (1) That *Demodex folliculorum* produces in dogs and other animals under certain unknown conditions a squamo-pustular eruption, and (2) that Gruby claimed to have produced disease in the skin of a dog by the inoculation of demodex obtained from a human being.

Perleche.

Perleche. Perleche has long been known and many monographs have appeared in the French and German journals, but thus far no monograph on the subject has been published either by the British or American dermatologists. It is, however, a disorder commonly encountered, and for that reason the paper of J. E. Lane[3] is a valuable contribution.

Perleche is occasionally found in adults, but it is preëminently a disease of infancy and childhood. It is an affection of the labial commissures, almost always bilateral, and usually rather closely limited to the commissures. As it progresses, the process extends for a varying distance toward the center of the lips, and usually extends a little on to the skin surface and on to the true mucous membrane of the inner side of the

(3) Jour. Amer. Med. Ass'n., July 21, 1917.

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lips. At the beginning of the disease the epithelium is smooth and whitish, with a mother-of-pearl tinge. As it progresses the epithelium becomes macerated, a little thickened, and loses most of the mother-of-pearl color. Small transverse fissures appear, which show a red base, if the lips be stretched, but which do not reach the lower layers of the epidermis, and which do not bleed readily even if rubbed. In some cases there is slight erosion, but the surface is ordinarily not denuded. One well known text-book on the diseases of children describes perleche as a "form of ulceration" and adds that "the ulcer is of a grayish color, is quite painful, and is associated with considerable swelling of the lip." According to other authors and to Lane's observations, this is exactly what perleche is *not*. It is never an *ulceration* and there is no swelling of the lips connected with it. There is little or no inflammatory area around the lesions. Occasionally a little of the pellicle can be detached and more infrequently there is some hypertrophy. As the lesions begin to heal their appearance approaches that of the early lesions and after the roughness has disappeared there remains only a slight discoloration which persists for a month or so. No scar is left. If treated, the disease is usually cured in two or three weeks. If left to itself there is usually spontaneous cure in a month or so unless there be re-infection, but in some cases the disorder is of definite duration. In one case which was left untreated the whitish color was still visible at the end of a year.

In the mild cases of perleche there is no symptom at all. In the fully developed cases there is a slight feeling of irritation which causes the child continually to run the tongue over the lesions. It is from this sign that the disease derives its name. There is never enough discomfort to cause the child to rub or pick the lesions. There is no other symptom nor physical sign. There is never more than the slightest local inflammatory reaction and the lymphatic glands are never enlarged. Impetigo, desquamation of the tongue and impetiginous stomatitis are sometimes associated with the disease, but in Lane's cases there was no such association.

Lemaistre considered perleche to be caused by a strep-

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tococcus which he called *Streptococcus plicatilis*. Several investigators following him considered the staphylococcus the causal agent. At present, all agree with the most recent writers, Cole and Jadassohn, that the streptococcus is probably the causal agent, but that it can not be considered absolutely proved to be such until we have succeeded in reproducing the disease in animals or human beings. Bartlett of Yale University made cultures from twenty of Lane's cases. Two or more varieties of bacteria were found in practically every case, but the streptococcus was the only one present in all cultures. This streptococcus in liquid media grew in long chains. On blood agar it produced a slightly greenish color, with little or no hemolysis. A few unsuccessful attempts were made to reproduce the disease in guinea-pigs with this organism.

Considering perleche as a streptococcus infection, many observers classify it as a variety of impetigo. Clinically this appears to be hardly justified, because the two diseases are not more frequently associated than may be accounted for by coincidence. None of these patients had impetigo though they were all in the class of individuals in whom that disease flourishes. In the lesions found on the skin surface, there was not the slightest resemblance to impetigo, and the cases of impetigo at the angles of the mouth bear no resemblance to perleche. In fact, impetigo usually stops at the edge of the skin, and does not extend on to the vermilion border of the lip. It would seem that if the diseases were identical, they would be frequently associated at the corners of the mouth, and that their appearance in this location would not be so entirely different. It may be, that while the streptococcus is an essential element in the causation of the disease, the association with it of some other bacteria is also essential, a condition of affairs somewhat similar to that found in Vincent's angina.

Perleche is highly contagious. Lemaistre found 312 of the 5,500 children in the primary schools of Limoges affected—slightly more than 5 per cent. Raymond describes two epidemics; in one, forty-two of the 155 children of one school were affected; in the other, twenty-five of the 245 children. Lane has seen five cases in

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one family, and two or three cases in several different families.

Common drinking utensils are the most frequent vehicles of transmission. Other ways in which it is spread are kissing and the use of common pencils, handkerchiefs and towels.

No careful observer would confuse perleche with any disease except syphilis. Perleche so greatly resembles the mucous patch or split papule that Fournier said that every practitioner who sees perleche for the first time never fails to mistake it for a mucous patch, and both he and Raymond asserted that the resemblance is so great that perleche is not to be differentiated objectively from the corresponding type of syphilis. However, this difficulty largely disappears if the mouth and the surface of the body be carefully examined, because secondary syphilis does not betray itself simply by mucous patches at the commissures. Lane's observations are in accord with these statements.

Lane says that his treatment is most simple. Prompt cure is effected by painting the lesions daily or every other day with a 10 per cent. solution of silver nitrate, a diluted tincture of iodine, and the copper sulphate or the alum pencil. Sabouraud recommends, in addition, an antiseptic mouth wash, but this is hardly needed in most cases. Auché found a 5 per cent. solution of chromic acid efficient in the few cases that resisted the milder treatments mentioned.

Sweat Gland Disturbances.

Hyperidrosis Circumscripta. Sutton[4] has had the opportunity to study a case of hyperidrosis circumscripta in which the symptomatology was striking in character and the anatomic changes well marked.

The patient was an Italian laborer, aged 28, who presented the general appearance of a rugged, powerful man. He claimed, however, that his health had never been good and his history during the past decade was that of a confirmed neurasthenic.

Aside from the diseases of childhood, and one attack

(4) Jour. Cut. Dis., March, 1917.

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of gonorrhea, he had never experienced a serious illness. There was no record of trauma. Syphilis was denied. The disorder from which relief was sought had been present eight years, and had reached its present stage within a period of a few weeks after the onset. Since then it had persisted with but little change.

The affected area measured about 8 by 18 cm. in extent, and was located in the left subscapular region. The sweating was more excessive in cold weather, but an attack could be precipitated at any time by fright, worry, or excitement. The phenomenon was not under the control of the patient's will, as in the case described by Marmé. Following the administration of pilocarpine, general hyperidrosis occurred, but the glands in the affected region were far more active than those on other parts of the body. On one occasion, during the course of a physical examination, more than 9 c.c. of sweat exuded from the affected area within a period of five minutes. The patient was not under the influence of any drug at the time, and the temperature of the room was 60° F.

Neither blood nor urine exhibited abnormal changes. A serum test gave a negative result. There was no reaction to tuberculin. No tenderness could be elicited by pressure along the course of the spine and an *x*-ray examination failed to reveal any changes or deformities in the bony structures in this region.

For laboratory study, four small pieces of tissue were excised from the affected area and four others from the corresponding normal area in the right subscapular region. The material was fixed in formalin, sectioned in a freezing microtome and stained by various methods.

The epidermis was unaffected and the sebaceous glands exhibited no alterations. The connective tissue in the vicinity of the coil glands and ducts stained well and, aside from occasionally circumscribed areas of round-celled infiltration, the intermediate structures appeared normal. The cellular exudate was most marked in the immediate vicinity of the coil glands and these structures were greatly increased in size—in many instances the diameter of the coils being almost twice that of the tubules in the normal specimens employed as con-

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trols. The blood-vessels likewise exhibited hypertrophic changes. The lumen of the enlarged glands was dilated and the epithelia somewhat larger than normal. Numerous mitoses were present. The ducts also were increased in size, although comparatively smaller than the active portion of the appendage. With the exception of the hypertrophy, the typical architecture of the glands was unchanged. There were no signs of fatty degeneration.

The microscopic findings in this case would indicate that in some instances, at least, as Virchow has stated, long continued localized hyperidrosis may result in, or be accompanied by, hypertrophy of the coil glands in the involved areas.

[We have had two similar cases under observation for several years. One of the patients, a young woman, has two areas on one hand.—EDITORS.]

Anidrosis Totalis. An interesting case of complete absence of sweat is reported by Lutembacher.[5]

The patient was a young woman who, when exposed to elevated temperature, developed intense vasodilatation instead of perspiration. Her general health was otherwise good. She passed through an attack of enteritis with a temperature which stood at 40° C. for several days without difficulty. No biopsy was obtained.

[Cases of mild xeroderma with little or no sweat secretion are not uncommon. In such cases, however, there is usually a generalized scaling, and a follicular papule due to a keratosis about the pilo-sebaceous orifice.—EDITORS.]

TELANGIECTASIA.

Hereditary Hemorrhagic Telangiectasia. In 1865, Babbington reported an interesting family in which recurring epistaxis had been observed for five generations. The transmission was through both male and female, but no mention was made of telangiectases in any of them. The first family in which these telangiectases were found was reported eleven years later by Legg, who described numerous small nevi on the face, forehead and trunk of his patient. The lesions developed in about the forty-

(5) Ann. derm. et syph., May, 1917.

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first year. These cases were followed by others reported by Chiari, Rendu, Osler, Josserand, Kelly, Hawthorne, Parkes-Weber, Phillips, Waggestt and Ballantyne. Rendu, however, was the first of these observers to associate the presence of epistaxis with multiple telangiectases as clinical manifestations of a distinct morbid entity. Henceforth, the erroneous diagnoses of hemophilia, acquired angiomas from cirrhosis of the liver, and hemorrhagic diathesis were no longer applied to this condition. Further interest in its study was aroused by the papers of Sir William Osler, whose first published article on it appeared in 1901. Most of these cases were carefully abstracted in 1909 by Hanes when he reviewed the literature on this subject and accurately described two additional families, so that fifteen in all were reported.

W. R. Steiner[6] has made a study of three additional family groups. From a consideration of the histories of these three families affected with hemorrhagic telantiectasis and those previously recorded, he concludes that heredity is the only important etiologic factor as yet discovered and that both sexes are equally affected and equally capable of transmitting the disease. Microscopically, a developmental defect was found in the dilated capillaries, as the elastic and muscle fibers appear to be wanting. The capillaries, consequently, are very likely to produce hemorrhages by their rupture, which is induced either spontaneously or by traumatism. The hemorrhages from the nose are generally seen early in life, while the telangiectases are a later development. The cautery in most instances offers the best results in the treatment of the bleeding telangiectases.

Scleroderma.

A Rare Form of Scleroderma. An interesting case of scleroderma showing some peculiar clinical features has been described by Ravogli.[7]

The patient was a man of 32, who began to experience severe rheumatic pains after a night of exposure. A

(6) Archiv. Int. Med., February, 1917.
(7) Jour. Cut. Dis., January, 1917.

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short time afterward the skin of the arms and legs showed rose-red patches, which were somewhat elevated above the normal skin, irregular in shape, hard, thick and without sensation. The face and the trunk were free from manifestations. The scleroderma began at the elbows as hard, round patches, which coalesced and formed a round, irregular patch at the radio-humeral joint, and another on the other side, at the ulnar-humeral joint. The skin was edematous and rose-red in color. The radio-humeral patch proceeded toward the middle of the flexor surface of the arm as a narrow stripe. The seat and the direction of this stripe corresponded exactly with the ramification of the radial and of the median nerves.

The same condition was shown in the legs, from the thigh to the foot. The sclerodermic patches covered nearly the whole anterior surface of the thigh, intermingled with which there were black, pigmented spots, while the posterior surface showed only a few patches. The skin was much more affected at the knee-joint, around the patella, appearing as rose-red, thick, diffuse patches, which were shown also on the anterior surface of the leg, reaching to the foot. At both knee-joints the sclerotic skin was deeply ulcerated, presenting round ulcers, some coalescing and forming long, irregular patches. On the right leg, the ulcers began from the patellar region and gradually extended to the inferior third of the leg. On the left leg, the ulcerated patches from the knee-joint ran down toward the internal surface of the leg. The ulcers had a thick, hard base, with elevated edges, covered with thick, hard, warty granulations, discharging scanty serum, the whole covered with thick, heavy crusts, formed mostly by epidermic scales. The ulcers were clearly of traumatic origin on a hardened, infiltrated skin, resembling somewhat epitheliomatous ulcers.

In this patient, the skin began to show alterations simultaneously with neuralgic pains of the peripheral nerves. The views of Singer, on the possibility of a disturbance of the internal secretions, seems not quite acceptable in this case. In the case reported by Singer,

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there was myxedema with scleroderma, and well-defined degenerative changes in the thyroid gland.

It may be possible that an affection of the suprarenal glands and the hypophysis, would produce alterations in the nutrition of the skin by their disturbed equilibrium; in this case, however, there was no symptom to indicate a disturbed condition of the glands of internal secretion.

It seems, in this case, judging from the degree of hardness of the affected skin and from the manner of onset, with severe peripheral neuritis, that there is some similarity to the case reported by Arning, under the name of erythema perstans pseudo-leprosum. The distribution of the scleroderma and the grouping of the patches show clearly the nervous origin of the disease. Substances may have been formed which produce stimulation of the vasomotor centers.

The relation of scleroderma to the distribution of the cutaneous nerves, in the form of stripes, as in this case, has been already observed by many authors, as Neumann, Crocker, Taenzer, Arning, and Thibierge.

In some cases, the distribution corresponded to a group of nerve ramifications proceeding from a spinal nerve (Bruns, Lion). In the same way, in cases of diffused scleroderma there is a tendency to symmetry, but in some cases the affection remains on one side only.

Nearly all authors agree that one of the exciting causes of scleroderma is a sudden change of temperature. In this case, the patient was caught in a thunder storm, and he remained the rest of the night with his wet clothes on. From this time, he began to suffer paresthesia and gradually the skin of the extremities began to show hardening. Nicholich, Brück, Andres, Ball, Gintrac and many others have reported cases in which scleroderma made its appearance after an exposure to severe cold.

One of the unusual features in this case was the occurrence of extensive ulcers in the scleroderma areas of both legs. At first glance they looked like epithelioma, but microscopic examination did not reveal definite characters of a new growth.

Cancer finds a good soil for its development in all tissues which have lost their reactivity. The skin af-

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fected with scleroderma, with its connective tissues hard, infiltrated, and affected by hyaline degeneration, is likely to ulcerate and also to show cancerous changes. Among the precancerous conditions, scleroderma must be mentioned.

SCLERODACTYLIA.

Sclerodactylia with Calcareous Concretions. Definitely formed cutaneous calculi, or calcareous concretions of the skin and underlying subcutaneous tissue, are of rather uncommon occurrence. G. M. Olson[8] reports this condition combined with sclerodactylia.

The patient, a young woman, aged 27, complained of circulatory disturbances of the hands and a markedly hard infiltration of the fingers. At various times ulceration had occurred with the extrusion of calcareous concretions.

The condition had existed for ten years, beginning with numbness and poor circulation in the fingers and hands. Later the fingers became stiffened, and hard masses, almost like fibromas, appeared in the tissues of the fingers, and near the olecranon. Some of the masses in the fingers had broken down and discharged hard, gritty, calcareous concretions.

An examination of the hands showed a very typical sclerodactylia, with all the fingers infiltrated and shiny. When exposed to the cold, the fingers appeared dead-white, blue-white or purple. The sclerodermatous infiltration involved especially the palmar surfaces of the first phalanges. On the palmar surface of the left thumb there was a circumscribed, hard nodule, and two large nodules near the left olecranon.

The patient had severe mitral disease and at one time the compensation had been poor. In general, however, she had been in good physical condition. She stated that at times the toes felt numb, but they showed no infiltration and were apparently normal.

The calcareous concretions varied in size from a pin head to a small pea. They were white in color, rather soft and brittle, and evidently composed very largely

(8) Jour. Cut. Dis., February, 1917.

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of carbonates, as marked effervescence occurred on the addition of nitric acid. Urates and uric acid were absent, showing that the concretions were not gouty in nature.

The calcareous concretions in the cases previously reported have varied in size from a small pea to 20 cm. in diameter. Chemically, they are composed chiefly of calcium carbonate, with some calcium phosphate. Urates and uric acid are always absent. These concretions have been found mainly in scleroderma of the fingers, although they have also been found in scleroderma of other regions, as the elbow, neck, knee, hip, and buttocks.

Eczema Seborrhoeicum.

Follicular Type of Eczema Seborrhoeicum. A peculiar type of seborrhoeic eczema is described by Trimble[9] which he says has not heretofore been recorded.

The type described was first noticed in its localized form; later it was discovered that, under certain conditions favorable for coalescence and spreading, it can become diffuse. The localized, or patch form, occurs commonly on the chest and upper back, as does the ordinary type of seborrhoeic eczema; it is extremely rare on the face, but has been noticed on the scalp, along the hair line, both in front and over the temporal regions.

Typical lesions of this variety, as seen on the chest or back, are patches that range in size from a silver dime to a half dollar; they are brownish-red in color, about the same as the usual lesion of seborrhoeic eczema, and are made up of a great number of inflammatory follicles, situated very close together, but always discrete. These follicles are slightly pink and enlarged, with dilated mouths; in each opening and around it, is seen a piling up of small, greasy scales, making a tiny cone; in fact, each individual follicle is a miniature lesion of seborrhoeic eczema. The grouping of a large number of such minute lesions makes up a patch of the so-called follicular type.

(9) Jour. Cut. Dis., January, 1917.

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Over the whole area the evidence of seborrhoea is apparent, and this is recognized by the usual slightly oily appearance. When this follicular type becomes diffuse, it will be observed that the mild thickening, seen in the local patch, has materially decreased; the infiltration seems to thin out as spreading takes place.

In the diffuse form, the eruption spreads gradually over the chest and back, until practically the whole upper half of the body is affected, with the exception of the face. At all times, however, the follicles stand out quite clearly, and the general appearance is one of a diffuse follicular disease of a seborrhoeic nature, associated with a moderate amount of furfuraceous scaling.

In an exaggerated case of long standing, the integument is rough to the touch, and in a mild sense takes on the nutmeg-grater appearance. It is cases of this type which bear some resemblance to a beginning lichen ruber acuminatus.

Cutaneous Manifestations of Hodgkin's Disease.

Skin Symptoms of Pseudo-Leukemia. The cutaneous symptoms of Hodgkin's disease may either precede, accompany or follow after the general manifestations, according to H. N. Cole.[10] Ziegler says that in from 5 to 12 per cent. of the cases, the cutaneous symptoms come first. Westphal says that in about 10 per cent. of his cases a lichen-like eruption preceded the onset. In some cases the skin lesions may accompany the generalized symptoms or, what is probably the most common type, they follow other signs of the systemic condition—it may be even from one to two years afterward and sometimes longer.

Probably the commonest of these symptoms is a pruritus of greater or lesser intensity. It is quite often the first sign to call the patient's or the physician's attention to the condition. It is sometimes so intense that deep grooves in the skin mark the imprint of each finger-nail; or, there may be a pruritus with abso-

(10) Jour. Amer. Med. Ass'n., Aug. 4, 1917.

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lutely nothing to be found on the skin. This symptom was noted eight times in Cole's series of thirty-four cases, and by Ziegler eight times in his series of seventy cases.

Marani says that he has observed a close relationship between pruritus and eosinophilia. Cole was unable to corroborate this, but found that these attacks generally came on with a fresh glandular "flare-up."

The next commonest lesion is a prurigo-like exanthem. These papular lesions, capped often with vesicles which are soon torn off by the scratching, are most often found on the extensor surfaces, but may be all over the body in a severe case. There are always more or less accompanying excoriations, scars and pigmentations. Often these lesions come and go for months. In Blaschko's case they disappeared when the throat lymphomas were removed, only to return later with recurrence of the latter.

Wechselmann, Nicolau and others report a diffuse exfoliating erythrodermia, though this is rather rare.

Urticaria has been seen in many cases of Hodgkin's disease. Kreibich reports a case in which urticaria preceded other evidence of the disease by six months.

Edematous swellings also are noted, and may be permanent or transitory in character. Pigmentations are seen frequently in lymphogranulomatosis, and are either spotted or diffuse. The brownish or bronze pigmentation is most often in the folds of the joints, abdomen, neck, face and extremities, and is much like that in Addison's disease, except that the mucous membranes are not involved. One also finds pin-head and larger chloasma-like spots on the arms, hands and face. The first type was noted in four of this series.

It is common to get a history of outbreaks of perspiration due to disturbance of the heat regulating functions. Disturbances in the nutrition of the skin, such as alopecia, dryness of the skin, atrophy of the skin, and hyperkeratosis, are also common.

Icterus is noted at times, and purpuric lesions are not uncommon.

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Grosz, Hecht, Ziegler, Bruusgaard and a few others also describe reddish or bluish tumors in the skin which, on being opened, have a bloody serous fluid, and are of a tissue typical histologically for Hodgkin's disease. This has been termed by Grosz *"lymphogranulomatosis cutis."* They are rare, and there was not one such case in Cole's series.

The author noted among thirty-three cases of Hodgkin's disease and one questionable case that there were thirteen involvements of the cutaneous surfaces. Pruritus was the principal complaint eight times, a prurigo-like exanthem was seen six times, a bronzelike pigmentation four times, petechiae twice, urticaria once, and edematous swellings three times. In one case the patient had an alopecia areata, and in another there were partially broken-down tumor masses in the left supraclavicular space, showing tissue histologically characteristic of lymphogranulomatosis cutis. In one case which was a probable lymphosarcoma the tissue became transposed into a leukosarcoma in the short space of a few weeks.

From an analysis of these cases and from the literature, Cole says that the skin lesions caused by Hodgkin's disease can probably be classified in two groups: (1) a true lymphogranulomatosis cutis, and (2) a group of lesions, set up, it is true, by the general infection, and yet not showing the characteristic histologic changes locally. A classification much like that of Audry's and Arndt's may be used for systematizing the dermatoses. Under the "pseudoleukemids" or "pseudolymphadenids" can be placed the purpuras, prurigo-like exanthems, pruritides, urticarias, pigmentations, and edemas. Some of them are disturbances of nutrition, as in Cole's case of alopecia areata, and some of them are cases of universal exfoliating erythrodermia. These lesions are a general result of the systemic infection, if such it be, on the entire system. The histologic picture, of course, varies with the condition, but in most cases shows nothing characteristic or possible of a diagnosis of lymphogranulomatosis. In a few words, it probably consists of a peripheral dilatation of the vessels, some edema of the tissues, and a greater or lesser small cell infiltration around the vessels, coil and sebaceous glands.

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PRURIGO.

Prurigo Following Splenic Radiotherapy in Lymphatic Leukemia. In the Year Book for 1915, Vol. IX, p. 43, an article by Kreibich was abstracted calling attention to a marked itching dermatosis developing in the course of splenic radiotherapy in a case of lymphatic leukemia.

Staumann[1] reports a similar case. When first seen, the patient, a man of 69, was emaciated and presented an indurated ulcer at the left labial commissure, which was found histologically to be of pure lymphoid structure. The leukocytes numbered 112,060, of which 94 per cent. were lymphocytes.

At the first seance, the lesions in the face and a group of submaxillary nodules were treated with deep radiation resulting in their complete disappearance in five days. Two months later treatment of the spleen was commenced with a dose of 3 H and a 2 mm. aluminum screen. Three days after the treatment, a papular prurigo-like itching dermatosis appeared on the legs and arms. The papules varied in size from that of a pin to a lentil, were of a pale pink color, and had in the center a small white point. Most of them were excoriated and crusted.

Histologically, these papules revealed well-defined cystic cavities in the mucous layer, containing cellular detritus and a few polymorphonuclear leukocytes and lymphoid cells. Surrounding these cysts the epidermis was edematous. Above, however, the granular and corneous layers were unchanged. The papillae presented edema and lymphoid infiltration particularly about the vessels.

After an interval of six weeks the radiation was repeated with a dosage of 2 H and the same screen. After three days, the itching papules recurred in greatly increased numbers, and the patient, convinced that the treatment had caused the dermatosis, refused further treatment. When seen six months later, the patient was found much debilitated. The treatment was repeated with the same result. After the pruritus had somewhat

(1) Ann. de derm. et de syph., May, 1916.

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subsided the spleen was again exposed to a 3 H dose, which resulted in an exacerbation of the itching papules.

The case is particularly interesting because it demonstrates that a clinically typical prurigo may be of lymphoid origin, due to a toxemia induced by radiotherapy of the leukemic spleen. Furthermore, the ulcerated lesion on the face suggesting both an epithelioma and a chancre is very rare although not unique, inasmuch as Nicolau[2] has reported a similar ulceration.

Schaumann confesses his inability to manage the case since radiotherapy can not be tolerated.

[In view of the excellent results obtained in some cases with benzene (benzol) this should be given a trial. —EDITORS.]

ELEPHANTIASIS.

Elephantiasis Nostras. According to the literature, elephantiasis nostras is a relatively rare condition as found in this country; in certain parts of Europe, however, it is less rare. For the most part the cases that have been reported were observed in England and France, but a few have been reported by German observers. J. A. Elliott[3] reviews the literature and reports an interesting case.

The trouble began about fourteen months prior to admission, when the patient, a young woman, noticed that the left hand began to swell, without any previous trauma. The skin was slightly reddened and felt warm to the touch. The swelling gradually progressed up the arm until the elbow was reached. At first there was no pain associated with the swelling, but later pain occurred in the fingers, elbow and shoulder. The erythema recurred at short intervals; the swelling, however, persisted from its inception, and did not subside to any noticeable extent between the attacks of erythema. Only a short while after the swelling appeared it was noticed that sensation was slightly decreased in both the arm and hand. At the same time the arm became mottled in appearance.

(2) Ann. de derm. et de syph., 1904.
(3) Jour. Cut. Dis., January, 1917.

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The left arm showed a diffuse symmetrical enlargement beginning at a point six inches below the acromion process when measured over the shoulder. From this point the normal dimensions gradually increased until the hand was reached, where the greatest enlargement was observed. It stopped very abruptly, however, at the distal ends of the first phalanges, and from this point the fingers emerged, normal in size, from the pouch-like enlargement (Plate III). The skin over the upper part of the arm was practically normal, and showed no distinct thickening; however, farther up the forearm the swelling appeared more pronounced, and there was definite thickening of the skin, which increased toward the hand. Over the back of the hand the swelling was very marked, giving it a "puffy" appearance. The skin over this region, as compared with that of the other hand, was about twice as thick, much firmer, and was distinctly dry and rough to the touch. Although greatly thickened, it was not fixed to the underlying structures. The skin over the fingers was firmer, and very firmly attached to the deeper structures, feeling almost sclerodermatous. Over the middle finger and forefinger, especially, there were numerous small nodules, which were boardlike in their firmness and gave one the impression of a fibroid tumor.

The entire arm was of a dusky red color, interspersed with small depigmented spots, giving it a mottled appearance. In these lighter areas there was almost complete anesthesia to pain. The patient, however, exhibited a somewhat decreased sensation over the entire body. The epidermis was roughened and covered with a slight scaliness. The hair follicles were depressed, and in places the skin was thrown into minute folds. Both on the back of the hand and on the palm there were numerous wart-like lesions, varying in size from a pinhead to that of a split pea, having the color of the surrounding integument. When incised, a small amount of lymph poured out from the incision.

Histologically, the epidermis showed only a slight thickening. The horny layer was about twice as thick as normal, loosely arranged, and in the upper layers there were a few unfinished horn cells.

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The corium was the site of very marked pathologic changes, the most striking of which was a tremendous increase in collagen, thrown into large bundles and whorls, and extending so far into the depths of the cutis so as to replace much of the subcutaneous fat. Around the deeper blood-vessels and sweat coils it showed a decided myxomatous and hyaline degeneration. Mast cells were extremely numerous, and seemed to be more in evidence where the collagen had undergone the greatest degree of hypertrophy—that is, in the deeper portions of the corium. These cells were pressed out into almost twice their normal lengths, and situated between the collagen bundles. In places, however, where pressure had been exerted from different directions, they assumed polygonal shapes. The papillae were flattened out, and rather far apart. The elastic tissue was decidedly decreased in amount. In the sections studied, hair follicles and sebaceous glands were lacking. There was an apparent increase in the sweat coils.

The larger arteries showed marked thickening as a result of proliferation of the endothelium, together with an increase in the thickness of the media. In places this thickening had progressed to such a degree that the larger arteries had very narrow lumina, while the arterioles and capillaries showed typical obliterative endarteritis. A similar change, but to a lesser extent, had taken place in the media of the veins, with but little change in the intima. The walls of the larger veins were sclerosed to the extent that they remained patent. Around all the vessels there was a marked infiltrate, which for the most part consisted of small round cell lymphocytes, with a good many polynuclear leukocytes and some mast cells. With Unna's polychrome methylene blue, cocci were demonstrated in small clumps around the vessels, just beneath the epidermis.

The etiology of elephantiasis nostras was not definitely known until Sabouraud published the results of his work in 1893. In a series of five cases he was able, by scarifying the skin during an erysipelatous attack, and culturing the blood and serum thus obtained, to demonstrate pure cultures of streptococci. All cultures taken between attacks, on the other hand, remained

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sterile. Since his work was published there has been much speculation as to whether tropical elephantiasis might not also be of bacterial origin. Prout has been one of the champions of this idea, and states that in his opinion both the sporadic and endemic forms of elephantiasis are due to the streptococcus. Dubruel seems to agree with Prout, as he concludes, after several years' study in the tropics, that the tropical form should be more closely allied to the sporadic form, and that it should be considered contagious during the erysipelatous attacks. He reached this conclusion after examining a number of the inhabitants of the Island of Moorea, where about 12 per cent. of the entire population are afflicted with this malady. He was able to demonstrate the filaria in only one case, whereas in many cases he found the streptococcus in pure culture or associated with staphylococci. Powell and Megaw both report similar results. While working in Bombay, Powell was unable to find filaria in a single one of seven persons afflicted with elephantiasis. On the other hand, he found 5 per cent. of a large number of the inhabitants examined to be infected with filariasis who were free from elephantiasis. Megaw examined 100 prisoners, three of whom had elephantiasis. Fifteen of the entire number were found to be infected with filaria, while all of the cases of elephantiasis were negative to filaria on repeated examinations. Manson still holds to his view that filaria is the essential factor in the production of the tropical type, explaining the presence of bacteria in the blood-stream, by the assumption that the filaria, by injuring the lymph vessels, predisposes to bacterial infection, the latter causing the lymphangitis and fever.

Disregarding the tropical type, it is definitely established that a majority of the sporadic cases are directly caused by the streptococcus. McDonagh believes, however, that syphilis may also be a direct cause, and cites a case to prove his point.

The etiology, while definitely agreed on by all, has been substantiated by very few. Sabouraud, as previously referred to, did the initial work in demonstrating the streptococcus of Fehleissen in his cases. Most observers who have reported cases since that time agree

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that their cases are undoubtedly of streptococcic origin, but they have failed to make either pathological or bacteriological studies. The sections studied in the author's case were biopsied during an attack of erythema and showed numerous cocci. Shortly afterwards, treatment was instituted and the erythema rapidly disappeared. At this time cultures were taken which remained sterile. This finding agrees with that of Sabouraud, inasmuch as all of his cultures remained sterile when taken during the non-erythematous period. The organisms found in the sections were in clumps, but occasionally a very short chain could be seen, consisting of from two to three cocci. For the most part they were seen just beneath the epidermis, situated around the blood-vessels and lymph channels, and especially where the infiltrate was most marked.

The symptomatology of elephantiasis nostras, according to Brocq, is characterized by recurrent attacks of erythema of the affected part. In some instances the initial attack is severe, and associated with general malaise, anorexia and fever. There is a marked edema with a definite lymphangitis, while the neighboring lymph glands are enlarged and painful. The inflammatory reaction of the skin subsides within a few days to a few weeks; the edema, however, tends to persist. The attacks recur at frequent intervals, until finally the edema persists from one attack to another.

Pain seems to be the second most constant symptom, varying between wide limits as to its severity. A probable explanation for this lies in the fact that the connective tissue has hypertrophied to such a degree that the nerve endings are pressed upon. In this case the pain in the fingers did not appear until the sclerosis was very marked, and the above explanation seems easily plausible.

The general pathologic picture in Elliott's case conforms to that generally accepted as typical. A few important findings, however, differ materially from those of other observers. In the first place, plasma cells are described by Unna as being present in large numbers, situated around the blood-vessels, while mast cells are numerous but not abundant. In these sections plasma

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Elephantiasis nostras.—Elliott (see page 56).

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cells were practically absent, while mast cells were very abundant. Again, the elastica was decidedly decreased, which has not been found in the experience of most observers, but emphasized by Unna as being very apparent in his experience.

The treatment instituted in this case consisted in baking the hand and arm in an arthritis oven for thirty minutes daily, followed by vigorous massage with petrolatum. The patient was given weekly intramuscular injections of antistreptococcus serum. Under this treatment the erythema disappeared, and the arm and hand had reduced about one-third in size when the patient left the hospital.

Epidermolysis Bullosa.

Epidermolysis Bullosa Hereditaria Köbner. Under this title has been described a very rare and peculiar skin affection, in which bullous lesions occur after mechanical but not necessarily chemical irritants.

Sakaguchi[4] of Tokio has made an intensive study of his personal observations and of other cases in Japan.

He found that the condition was hereditary in ninety-five of the cases in the literature and in nine of the fifteen Japanese cases. Consanguinity of the parents occurred in four of his fifteen cases and in numerous cases in the literature.

The fact that the disease is found among negroes and Mongolians disproves a former contention that the condition was peculiar to the Germanic races.

Of the 401 previously reported cases there were 223 males and 139 females with no mention of the sex in thirty-nine cases.

The condition is rarely present at birth; it begins as a rule in early childhood, but may come on in cases late in life. In the author's series it occurred in two cases at birth, in five cases in the first two years, in one case in early childhood and in one case at 24 years of age.

Hyperidrosis, with aggravation of the condition in hot weather, occurred in five cases. In nine cases hyper-

(4) Archiv. f. Derm. u. Syph., Vol. 121, p. 379

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idrosis was absent, nor was there any seasonal change in these.

Secondary skin changes, such as atrophy, scars, pigment abnormalities and milia-like formation, were present in all the author's cases. Nail and teeth malformations were frequently encountered.

Bacteriologic investigations were invariably without results. The blood, including the Wassermann reaction, showed no pathologic changes.

The bulla formed in all cases by a lifting of the epidermis from the derma. The common histologic picture was an edema of the upper corium, emigration of cellular elements, dilatation of the vessels and constant absence of elastic fibers. The melia-like borders were due to obstruction of the sweat-gland ducts, and in some cases, also, of the pilo-sebaceous ducts.

The most striking feature of the disease is the separation of the epidermis from the corium. In many cases Nikolsky's sign was present. It is an interesting fact that chemical irritants were without effect. The application of blister-plasters caused less reaction, and after a longer time than on normal skin. Neither electrical current, Roentgen ray, nor Finsen light caused bullous formation. Application of heat or plunging the finger in hot water usually caused merely an hyperemia.

The general condition of the patient was in all cases good, aside from anemia in a few individuals. In four cases improvements occurred with age. Intercurrent infections were without influence on the disorder.

The author considers the disease as an hereditary unstable union between epidermis and corium, and a tendency toward capillary edema due in many cases to consanguinity of parents.

The different forms of the disease are but different grades of the same disorder. He suggests "Epidermolysis bullosa hereditaria traumatica" as the best descriptive term.

Sakaguchi has found no treatment to be of any value.

Epidermolysis Bullosa with Loss of Elastic Tissue.

A case of epidermolysis bullosa is described by R. S. Weiss[5] lacking the hereditary but having the congen-

(5) Jour. Cut. Dis., January, 1917.

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ital features, which showed loss of and changes in the elastic tissue of the apparently normal skin. This anomaly was first reported by Engman and Mook, and later confirmed by Kanoky and Sutton.

The opinion of Engman and Mook that the probable etiologic factor in epidermolysis bullosa is the diminution or absence of elastic tissue is again confirmed.

Neoplasms.

Primary Non-pigmented Sarcoma of the Skin. Primary, non-pigmented, isolated sarcoma of the skin is of relatively infrequent occurrence. The majority of dermatologists have seen but few cases, if one may judge from the scarcity of reports on the subject. Advanced sarcomas of the skin and subcutaneous tissues are more frequently encountered by the surgeons because of the large size attained by these growths and the necessity of surgical removal.

Two cases of isolated primary sarcomas in young adults have been studied by Joseph Zeisler and E. P. Zeisler.[6] In one case the lesion occurred on the chin of a young woman 21 years of age. Histologically, the predominating cells were seen to be typically spindle-shaped, with large vesicular nuclei, distinct nucleoli and tapering protoplasm. Many small multinucleated giant cells were present containing from six to twelve deeply stained oval nuclei centrally situated and surrounded by a narrow rim of cytoplasm. In the deeper layers of the tumor were found larger giant cells with from thirty to sixty ovoid nuclei peripherally arranged around a clear central zone. No mitotic figure was found. Elastic tissue was absent. All the normal glandular and collagenous structures of the corium had been destroyed and replaced by the tumor cells. On account of the clinical resemblance of the tumor to xanthoma, sections were stained with Sudan III and osmic acid. None of the characteristic fat-containing xanthoma cells was found. The histologic diagnosis was a primary spindle cell and giant-cell sarcoma of the skin.

A careful search for similar cases in the literature

(6) Jour. Amer. Med. Ass'n., July 14, 1917.

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convinced the authors that a true giant-cell sarcoma of the skin, that is, one in which giant cells are present in large numbers and are an essential element in the development of the tumor-like spindle or round cells, must be very rare. Pathologists have not definitely determined the origin of the giant cells in sarcoma. Mallory suggests that there are two types of giant cells: (1) The giant cell due to multiple mitoses, signifying rapid proliferation under favorable nutritive conditions and representing a true tumor cell, occurring in some forms of fibrosarcoma, and (2) the giant cell due to fusion of endothelial leukocytes attracted to the tumor by foreign bodies like fat crystals or lime salts around which they have fused. This type is found in the so-called giant sarcoma of bone and in "epulis" tumor of the lower jaw, which is thought by some pathologists to be inflammatory tissue full of giant cells. A few instances of giant-cell sarcomas outside of the skeletal system have been recorded in the tendon sheaths of the hands, the uterus, mammary gland, and the subcutaneous tissues. Some of these cases, described as myelomas of the tendon sheaths, have been found to contain cholesterol and therefore belong to the xanthomas. In every case of sarcoma of the derma or subdermal tissues containing large numbers of giant cells, some possible connection with the underlying bone substance should be sought for in accordance with the theory of embryonal rests or embryonic defects.

In the other case the lesion was situated near the elbow of a young man 22 years of age. Histologically the tumor was found to be a pure spindle-cell sarcoma of the cutis undergoing ulceration in its early stages. The interesting feature of this case was that it represented a primary spindle-cell sarcoma, developing apparently in normal skin after an injury. No giant cell was found.

The writers advise early excision to prevent dissemination.

Multiple Benign Tumor-Like New Growths of Schweninger and Buzzi. Schweninger and Buzzi described, under the name "multiple benign tumor-like

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Photomicrograph showing hernia-like projections in center of tumor.—Pusey. (see page 66)

Benign neoplasms of Schweninger and Buzzi.—Pusey. (see page 64)

PLATE IV.

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new growths," a case showing a unique anomaly of the skin (see Plate IV).

Pusey[7] describes a case which agrees closely with the description made by Schweninger and Buzzi. Pusey has been unable to find in the literature any other cases of this peculiar condition.

The patient was a man 37 years of age who had had small, almost flat, scar-like spots and oval swellings from the size of a pin head to that of a hazel nut on the chin, face, arms, back and buttocks for the past fifteen years.

The lesions first appeared on the chin, and were noticed on the back about three years later. They have slowly increased in number since. The patient thinks that the lesions attain their full size in a few months and subsequently do not enlarge. Many of the flattened lesions look as though they might have shrunken. The atrophic character of the lesions, however, would account for this appearance, and as far as the patient has observed there has been no shrinkage of the lesions. Their appearance and their subsequent course have been absolutely unassociated with subjective symptoms.

The lesions varied from slightly elevated, small spots to hemispherical, bulging swellings, which looked as though at these points there was loss of strength in the skin so that it yielded to the pressure beneath. The lesions on the chin are well shown in the accompanying illustration. These, as well as the lesions elsewhere, are much more distinct by side light than by direct light. A side light is necessary in order to see the smaller lesions clearly. They are raised, oval or hemispherical tumors, but they are as soft or softer than the normal skin, and are on the stretch. When the pressure is removed they immediately resume their original shape. The patient's barber had noted that the masses flattened out under the razor, and that there was no difficulty in shaving over them. The skin over the lesions on the chin is of normal color or occasionally shows a faint slate color or reddish tinge. In the larger lesions some dilated blood-vessels are visible. The hair follicles show no visible change. The lesions on the chin are the largest that exist except those on the buttocks.

The lesions on the upper lip are few and of the same appearance as the smaller lesions on the chin. Numerous very slightly elevated lesions are found on the forehead. On the face, as elsewhere on the body, the eruption is evenly distributed on the two sides.

On the back, the lesions occur in an area extending at the midline from the third dorsal to the second lumbar vertebra, and from the posterior axillary folds to the crests of the ilia. The lesions here are not globular, but are oval or

(7) Jour. Cut. Dis., September, 1917.

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linear patches, very slightly raised above the level of the surrounding skin, and look like thin scars or slightly raised blisters. Many of them are visible only by side light. In size they may vary from a pin head to that of a finger-nail, and they are arranged with their long axis following the cleavage lines of the skin. Some of them are distinctly whiter than the normal skin; they look, in fact, like the white scars that result when bits of skin are clipped out to make skin grafts. Other lesions, particularly the larger ones, are of a light yellowish brown color. In the larger lesions the surface has a cigaret-paper appearance, and the fine markings of the skin are accentuated. Some of the lesions show a few dilated follicles on their surface, but none of these follicles appear as blackish points, as described by Schweninger and Buzzi in their case.

The lesions on the arms are similar to those on the back, and are confined to the extensor surfaces of the upper half of the arms. There are no lesions on the forearms or hands.

On the buttocks, the lesions are very numerous, and are largest, some of them having a long diameter of about 2 cm.

At the sides of the neck, back of the ears, the skin is mottled by small oval spots, 4 mm. in long diameter which are slightly lighter in color than the surrounding skin. While their elevation can not be made out—on account of the fact that they are covered with hair—there seems no reason to doubt that they are lesions of the same character as those existing elsewhere.

The lesions show no disturbance of sensation.

Histologically, the epidermis was found practically unchanged. In the corium, however, the histologic picture was found to compare closely to that described by Schweninger and Buzzi.

The striking features were first, a marked loss of elastic tissue in the involved area, and second, an infiltration of round cells about the blood-vessels. The most marked change in the elastica was in the papillary and subpapillary portions. Differential stains showed a complete loss of elastic tissue here. In the deeper layers of the corium there was also a considerable diminution in the number of elastic fibers, and those remaining were broken and fragmented. Beyond the border the elastica was normal. An increase in its amount at the border as described by Schweninger and Buzzi was not apparent. The part in which the most complete involvement occurred is well demarcated from the surrounding skin in two ways. First, by the fairly sharp beginning of the loss of elastica; and second, by the bulging outward of the epidermis; the latter was undoubtedly due to the fact that the skin, weakened by the absence of elastica, yielded somewhat to the pressure beneath and was pushed out in a hernia-like swelling.

The cellular infiltrate occurred particularly and almost exclusively about the vessels. The infiltrate was confined for the most part to the vessels of the superficial layer of the

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cutis. It did not occur around the sweat and hair follicles, as in Schweninger and Buzzi's case. The cells of the infiltrate were for the most part, of small round-cell type, although there were also a considerable increase above the normal in most cells and plasma cells. Aside from the loss of elastic tissue and the perivascular infiltration, the corium was normal.

Pusey believes the condition to be due to a congenital defect in the skin—one characterized by failure of development of the elastic fibers in minute areas of the skin; this lack of elastic fibers in the upper part of the corium results in a weakening of the corium and a consequent bulging in these areas. The appearance of the lesions only in adult life might readily be accounted for by the fact that the weakness in the structure of the skin might not be sufficient to cause it to manifest itself in the youthful skin, but would show itself by yielding at the points of defective structure as the skin lost its youthful tone. The slight cellular infiltration in the skin might be accounted for by the injury to the tissues which resulted from their giving way. A similar infiltration may be found in linea albicantes, which are in a way, analogous lesions. A congenital defect of development of elastic fibers is not an unknown occurrence. Engman and Mook have shown that there is a congenital lack of development of elastic fibers in the papillary layer in epidermolysis bullosa.

Analysis of Forty-three Cases of Skin Cancer. In an analysis by S. E. Sweitzer[8] of forty-three cases, there were twenty-eight males and fifteen females. This is nearly twice as many in the male as in the female. The ages varied from 27 to 86 years; there were two patients under 30; seven under 35, eleven under 50, and thirty-two above 50 years. The duration of the disease varied all the way from eight weeks to twenty-five years.

The lesions were all located on the face, neck or ear. Most were around the nose or on the cheeks. The lower eyelid was involved twice, the temple twice, and the lower lip four times. Of the lower lip cases, two were due to smoking, one to a cold-sore and one to seborrhoeic keratosis. We all know the malignancy of cancer of the lower lip, but cases involving the inner canthus of

(8) Jour. Amer. Med. Ass'n., July 21, 1917.

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the eye are very hard to cure, and if they involve the orbit, the difficulties of treatment are greatly increased.

From the frequency of the occurrence of skin cancer on the exposed surfaces of the body, one is led to believe that the rays of the sun may have something to do with its production, or it may be only on account of the better opportunity for irritation to occur.

Fourteen of these forty-three cases were due to seborrhoeic keratoses. This is about 30 per cent. and is the most frequent cause in this series.

Acute injury, such as a razor cut, or a scratch, or being hit with a stick, was responsible for seven cases, and three cases were directly due to pinching out a blackhead with the fingers. This gives ten cases due to an acute injury and is about 25 per cent. of the total. Most writers mention trauma as a cause, the occurrence of repeated slight injuries, but do not emphasize the single injury.

Other causes were warts in three cases, pimple five cases, smoking two cases (both of which were on the lower lip), cold-sore two cases, scaly spot three cases, irritation of nose-glasses one case, irritation of alkali dust one case on lower eyelid, angioma one case, and red spot one case. Every one of these cases then was due to either one acute injury or to a precancerous dermatitis or to chronic irritation. The high percentage of cases due to an acute injury would lead one to suspect either an infectious origin or a displacement of cells at the time of injury.

In patients with seborrhoeic keratoses, the formation of skin cancer is possibly aided by the irritation of sunlight, scratching the lesions and picking off the crusts. This might explain the cause of the occurrence of skin cancer in these patients only on the exposed surfaces. One often sees seborrhoeic keratoses on the body, but Sweitzer has never seen a skin cancer on the body caused by it.

There were seven patients with multiple lesions, and of these six were due to seborrhoeic keratoses and the other was due to a scaly spot.

The treatment given in these cases was radium. Thirty-four patients are cured to date; four are still

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under observation and should result in cures; two were benefited but are not well yet; two had recurrences and one patient was directly stimulated. Of the two cases that recurred, one involved the neck and was previously treated with the Roentgen ray, but not entirely healed. This patient has done well under radium, but is not completely cured.

The second patient also had received Roentgen treatment, in this instance extending over a period of nearly three years. After one course of radium treatment the patient disappeared for six months, and the disease, which previously was on the bridge of the nose, had spread so that it involved the frontal sinus. This patient had in previous years been operated on twice and the lesion had recurred both times.

The case that was directly stimulated involved the malar bone and the amount of radium used was too small to be effective. It was necessary to resort to surgery and do a wide operation, and Roentgen rays were used afterward. This patient writes that he is now apparently well. This was a prickle cell tumor.

[In our experience the epithelioma of the inner canthus has not shown itself to be unduly resistant to Roentgen ray. Ascribing an acute, minor injury as the cause of epithelioma is in many cases due to faulty observation on the part of the patient. Careful inquiry will oftentimes show that the injury merely served to call attention to a pre-existing keratosis. A "pimple," said to be the forerunner of the epithelioma, is usually found to be the neoplasm itself.—EDITORS.]

WAR DERMATOSES.

Common Skin Affections in Soldiers. Medical men in charge of patients in military hospitals, convalescent homes and camps are often called upon to diagnose and treat certain diseases of the skin. Contrary to what one might expect as a result of the conditions under which a soldier lives on active service, the list of these complaints is not a long one says H. G. Adamson.[9] Eczema, in the production of which local irritants are

(9) Lancet, Feb. 10, 1917.

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known to be a prominent factor, is by no means common among soldiers, in spite of infrequent baths and change of clothing. On the contrary, many men who in civil life have been victims of eczema, have lost that complaint while serving in the army. Neither does one see, as again one might expect to see among those who have been at the front, lichen planus, an affection which in civil life is often caused by stress or nervous worry. The really frequent skin affections of soldiers are comprised among the more common contagious skin diseases. Pediculosis, scabies and impetigo contagiosa are probably the most prevalent after which come certain forms of ringworm. If we add to these the eruptions of secondary syphilis and psoriasis vulgaris, these half-dozen affections are those with which a military doctor is most likely to meet.

Pediculosis is mainly a complaint of the trenches, and, as "the louse problem of the western front," its management has been fully discussed in the medical journals. Syphilis is a disease which at once passes out of the hands of the local medical officer to be treated in special hospitals for venereal diseases.

Scabies, impetigo contagiosa and, to a less extent, ringworm, though in a sense trivial complaints, are nevertheless responsible for the temporary invaliding of hundreds, perhaps thousands, of otherwise able-bodied men. Measures for the treatment of these diseases are therefore worthy of attention. Psoriasis also invalids many otherwise healthy men and sends them to hospitals either because of the extent and consequent discomfort of the eruption, or because the eruption is looked upon with suspicion by the man's companions.

It is a very good rule, when a soldier (or, indeed, a civilian), of whatever rank, complains of itching, to think first of scabies, and to exclude that disease before giving consideration to any other. Itching at night is particularly suggestive of scabies.

One looks between the fingers, about the wrists, and particularly on the penis, for "burrows," and for red raised ridges, the result of burrows which have become inflamed by scratching or infection.

On the fingers and wrists the burrow is seen as a

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narrow wavy line, generally black from included dirt, and from 1/16 inch to 1/4 inch long. Sometimes there is near, but not actually at one end of, the burrow a clear pin-head-sized vesicle—the pearly vesicle—over the roof of which the burrow passes. When examined with a lens the acarus can be seen at one extremity of the burrow as a whitish speck like a minute smooth flat pebble imbedded in the skin. When seen it can be easily removed by touching it with the point of a darning needle, and examined under the microscope in a little liquor potassae, and the diagnosis is certain once for all. This is the only sure way of finding the acarus; to grope for it blindly in the burrow or the pearly vesicle is useless.

[A more simple and more certain method of finding, not only the acarus, but the ova and excreta as well, consists in removing the entire burrow, or, if a new and solitary lesion, the vesicle, by means of a thin and very sharp blade. The tissue is then inverted on a slide and examined in liquor potassae under a cover slip.—EDITORS.]

The simplest and most efficacious treatment is as follows:

(1) ℞ Saponis mollis ..... 700 gm.

(2) ℞ Ung. sulphuris ..... 700 gm.
S. The soap and ointment for three applications.

1. A hot bath of half-an-hour's duration is taken on three consecutive days. During the bath the body and limbs, especially the hands and wrists and buttocks, are scrubbed with soft soap by means of a flesh brush.

2. After each bath the patient himself rubs in the ointment and puts on an old sleeping suit, gloves and socks and goes to bed, where he remains until it is time for the bath on the next day.

The baths and inunctions must on no account be continued beyond the three days. The patient gets up and dresses after the three days and usually requires no further treatment, but is kept under observation for another three days. If, as sometimes happens, some itching continues he is given the following lotion to mop on night and morning.

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℞ Liq. picis carbonis..... 1 dr. (4 c.c.)
Aq. ..... 20 oz. (600 c.c.)

If the treatment has been thoroughly carried out the patient is cured and free from infection after the three baths and inunctions. If a case be not cured in this way, it is probably not scabies, but either a papular urticaria or chronic eczema. For the former affection a lotion of ordinary vinegar is often efficacious. For the eczema a zinc ointment should be freely applied and all baths forbidden.

By this method of treating scabies, with one bath and a good supply of hot water, from twelve to sixteen men can have treatment each day, or a complete cure for from twenty-four to thirty-two men per week, and so on, in proportion to the number of baths available. Clothes may be disinfected, but in practice this is found to be unnecessary. Brushing and airing of outside clothes and washing of underclothes suffice.

It has been already remarked that impetigo may complicate scabies and that it then attacks particularly the hands, buttocks and thighs. But it often occurs apart from scabies, as single cases or in small epidemics.

Its usual situation is then the face, beard region and scalp, and the fingers. It is of common occurrence as a result of a visit to the barber or from using a public towel. It usually begins on the beard region as scattered isolated crusts, which quickly spread on to other parts of the face, about the ears, and sometimes on to the neck and scalp. It is often mistaken for sycosis or for eczema, but it is easily recognized by the appearance of "stuck-on" amber-colored crusts from the size of a split pea to that of a shilling. Each of these crusts represents the dried serum of a blister, but the drying takes place so quickly that the original blister is seldom seen, though on removing a crust with forceps there is revealed a raw weeping surface, which is the base of the blister. Frequently there is a phlyctenular whitlow on a finger or thumb around the root of the nail, and there may be crusted patches on the hands or forearms.

The patient should be made to mop off the crusts with a wad of wool (absorbent cotton) and hot water, and to continue to mop for half an hour or until every crust

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is removed. A lotion of 1 in 6,000 mercury bichloride is then daubed on for a few minutes and a diluted white precipitate ointment applied. The bathing and application of ointment is repeated several times daily and continued until no fresh crusts are formed. In this way the most extensive eruptions can be cured in a few days. Without the thorough removal of crusts the ointment fails to reach all the infected parts and the eruption continues.

Ringworm is a third contagious skin complaint which may incapacitate soldiers, though it is less generally prevalent than either scabies or impetigo. It may occur on the beard region or on the forearms in the form of large disc-like inflammatory plaques with pustulating points as the result of infection from horses, and epidemics of "horse-ringworm" of this sort were at one time prevalent in certain cavalry camps, but have apparently now ceased to occur.

More general forms are ringworm of the groin (tinea cruris or Dhobie itch) and eczematoid ringworm of the extremities. Groin ringworm is perhaps more often met with among officers, and ringworm of the toes and feet particularly in hot climates or during warm weather. Ringworm of the groin and the interdigital ringworm may sometimes be associated in the same patient. Ringworm of the toes and feet calls for most attention because it is less generally known and recognized as such.[1] In its mildest form it causes red, dry, or excoriated surfaces between the toes due to peeling off of the horny layers of the epidermis. The red surfaces are sharply margined from the normal skin by an overhanging fringe of epidermis, and they generally extend on to the sole of the foot. In cold weather it often remains in this condition and causes comparatively little discomfort. In hot weather, and in tropical climates especially, the eruption may spread rapidly and extend over the foot and even up the leg to the knee in the form of blisters and excoriations, sometimes with edema of the leg. Many such cases were seen invalided from Gallipoli.

(1) Ormsby and Mitchell: Practical Medicine Series, Vol. IX, p. 65.

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One of two measures may be adopted in treating any of these forms of ringworm.

1. The application of an ointment which we owe to Whitfield, viz.:

℞	Acid. benzoici	2 gm.
	Acid. salicylici	4 gm.
	Ol. coca-nucis	12 gm.
	Vaselini ..... ad	30 gm.

In cases in which there is vesication the inunction should be preceded by fomentation with hot water. Many cases quickly clear up with this treatment, but sometimes part of the eruption in the groin, or between the toes, or on the soles, remains obstinate, and for these cases a useful treatment is:

2. First thoroughly mop the affected parts with tincture of iodine; then rub on silver nitrate 0.6 gm., spirit of nitrous ether 30 gm. Repeat this treatment if necessary, and apply the benzoic acid ointment in the interim.

For the treatment of psoriasis in soldiers it is but waste of time to try internal remedies. They are generally disappointing, and, in any case, show no results for weeks. It is better at once to apply local remedies. The following ointment is often successful in removing the eruption:

℞	Hydrarg. ammon. chlor.	4 gm.
	Liq. picis carbonis	15 c.c.
	Ung. paraffin. B. P.	180 gm.

S. The ointment to be well rubbed in twice daily with a piece of flannel.

This ointment, which is made with a stiff base—unguentum paraffin—is usually more effectual than when made with simple vaseline. If this ointment fail chrysarobin ointment (B. P.) should be employed, with the usual precautions of avoiding the face, hands and scalp, and relaxing the treatment if chrysarobin erythema appear at any part. The patient should be kept in bed when chrysarobin ointment is used.

The treatment of psoriasis usually will be slow, but for most of these complaints it may be said that with prompt and efficient treatment the period of hospitaliza-

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tion will be reduced to a week or so, while inefficient treatment may prolong that period to many weeks or months, or lead even to eventual discharge of men from the army with the complaint still uncured.

Dermatology on Active Service. Wettenhall,[2] of the Royal Army Medical Corps, gives a good account of the occurrence and management of the various dermatoses both in England and at the front.

In the Aldershot command (England) there were two General Hospitals, with a dermatologist at each. All patients with venereal disease were sent to one of them, and at this hospital there was an assistant responsible for syphilitic cases. There were also wards for scabies, attendants for these cases, and special baths. *X*-rays were available for treatment, but were in charge of the skiagraphist.

The isolation hospital, with over 500 beds, received patients with infectious exanthemata.

At the front the medical officer of a unit carried his equipment on a Maltese cart, and usually found comfortable inspection rooms. Any reasonable need could be obtained by requisitioning the field ambulance. In the trenches, a dug-out and first-aid was all that was available. The field ambulances were housed in substantial buildings as a rule, rapidly transformed for hospital use, and there they undertook treatment of temporary conditions, such as scabies.

There were three field ambulances to each division, so that each field ambulance cared for approximately 5,000 men.

In each division, too, there was a sanitary section, with a medical officer in charge, and baths were arranged, where clean underclothing could be obtained and the clothes were ironed when infected with pediculi.

Infectious diseases were sent to special hospitals, and venereal diseases to a special camp at the base, as also were self-inflicted injuries.

Official military manuals give directions clearly and concisely to all branches of the service in such matters as first-aid for burns and on sanitation.

Pamphlets are issued with directions for prevention

(2) Med. Jour. Australia, March 3, 1917.

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of such new conditions as trench feet, and strict orders are given that the precautionary measures should be carried out by the commanding officer. This, of course, is necessary, as the medical officer of a unit is only an advisor to the commanding officer, and is not officially responsible for his advice being carried out. When a man is put on the sick list, then the Royal Army Medical Corps takes charge of him, but not before.

Abroad, of course, accommodations varied from bedrooms (rarely) to barns in various stages of repair, and the trenches with their dug-outs, which were, as a rule, infested with mice and rats. Clothing was excellent and diet adequate. Troops are not left long in the same billets, and have to clear up on leaving; they are fully exercised when in back billets by road marches. The medical officer finds that care of the men's feet is an important part of his duties with the infantry. There is an excellent official manual on chiropody; one or more men are trained as chiropodists to each battalion, and a special set of instruments is provided. In addition there are boot-makers, so that alterations and repairs can be made on the premises, so to speak. Numerous men with hammer toe served without difficulty.

It was difficult to get some men to wash their feet, as the idea prevailed that doing so softened the skin; but where the feet perspired freely, bathing and frequent changing of socks were necessary. Boots were softened with castor oil, and were made to fit well round the ankle, with plenty of room for the toes.

The author saw no trench foot, although the men were as long as ten days in the trenches at a period, and snow was on the ground continuously for six weeks. The condition was described and measures for its prevention laid down in special pamphlets issued for the army.

One pest is the ever-present louse. *Pediculus capitis* was practically absent; the men's hair was kept short, but not shaved. *Pediculus pubis* was there sometimes, very strongly entrenched; but *Pediculus corporis* was the general variety found. Its spread was helped by the fact that men could not retain their own blankets when

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marching, as their packs were too heavy. Consequently, their blankets got mixed on the wagons which carried them from place to place. As frequently as possible the men were given hot baths and a clean change of underclothing, and infected trousers were ironed along the seams to destroy the eggs. Infected clothing was treated by Thresh disinfector. A whole company was paraded at one time for inspection, and passed by in single file, with neck and shoulders bare; the affected men could readily be singled out by the excoriations.

Cases of German measles occurred sporadically through the winter, and though isolation of contacts was carried out as often as possible, it was not very successful. Minute particulars of each case had to be reported to the Acting Director of Medical Services of the Division, and disinfection of the billet was carried out by the sanitary section.

The absence of syphilis was notable amongst the troops both in France and at home.

There was no scurvy nor any condition of an allied nature, as there was an abundant supply of potatoes and fresh meat in the diet; bully beef and Maconochie's rations were issued, the latter often being a mixture of vegetables and meat in 1-lb. tins. Some attacks of diarrhea were put down to this ration, but the author saw no skin affection caused by food poisoning.

One case of recurrent facial edema occurred in the carpenters employed with the battalion; but it was due to external irritants.

Onychia, with an associated lymphangitis, occurred in a few cases, but by removing the nail and applying antiseptic foments it was unnecessary to send the patients to hospital.

Eczema was rarely encountered, but seborrhea was not so rare. Kerion occurred sometimes, no doubt derived from the horses, as those men affected were in the transport service. One case of epithelioma was seen in a middle-aged man who had an old wart on the palm of his hand.

A generalized mercury dermatitis followed the rubbing in of *unguentum hydrargyri* for *Pediculi pubis* in

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two cases. Urticarial and erythematous conditions were seen after inoculations for typhoid, but not very frequently. Psoriasis occurred in a few cases. The men were not taken off duty, save when this affection was severe.

Impetigo contagiosa was not rare, but by strict treatment was prevented from causing much trouble. Artificial eruptions were not encountered, though self-inflicted injury was not unknown. In only one case did intertrigo of the groin give trouble; the man did not report sick until on the march.

The dermatological wards at the general hospital at home were occupied mainly by scabies, which was treated very successfully with balsam of Peru derivative instead of sulphur. Eczema, psoriasis, impetigo contagiosa, sycosis and syphilis were the principal other conditions.

The eruptions in cerebrospinal fever were not so frequent as we are sometimes led to expect, and the marked purpuric eruption was the exception rather than the rule.

Occasionally cases of flea-bites were sent up as German measles, and a case of erythema multiforme was sent as cerebrospinal fever.

Vincent's Infection Involving Mouth, Eyes and Penis. Since publishing a preliminary report on "Infectious Stomatitis Among Troops" in 1916[3] many cases of this serious condition have been seen by Bowman.[4] That cited here is of sufficient interest to warrant an individual report.

The patient was a captain, 30 years of age. About March 1, 1917, he noticed that he began to lose his voice. He described no pain in connection with this, but it seemed to be due to a sense of constriction in the throat. The glands in the neck were not tender. The condition gradually became worse, and on March 15, while instructing a party in trench work at night, he had a severe chill and a cough developed. He then noticed soreness of the eyes with watering, and had great ten-

(3) Proc. Soc. Med., 1916, Vol. 9 (Medical Section), pp. 51-60.
(4) Lancet, Oct. 6, 1917.

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derness of the gums. On March 19 he was admitted to hospital.

On admission the temperature was 102° F. The patient was greatly depressed, felt chilly, and could eat nothing but fluids because of the soreness of the lips and inside of the mouth. Examination showed a very severe conjunctivitis, with a large amount of thin discharge present containing flakes of whitish material. The conjunctivae were red, with a certain amount of photophobia. The mouth was half opened and the lips covered with angry herpetic-looking ulcers, some of which were covered with a fragile whitish membrane. These seemed to be confined to the lips, and had not extended to the surrounding skin. On account of the pain it was impossible to open the mouth, and it was very difficult to retract the lips. The gums were reddened, the teeth bathed in pus, and pressure on the gums caused severe bleeding. The hard palate was covered by a whitish membrane, which came away easily, leaving a bleeding surface. The throat, which could be seen only partially, was covered with a membrane also, but there was no evidence of any deep ulceration. Smears were made from the eyes and from the ulcerated areas in the mouth, as well as from the gums. These showed large numbers of Vincent's organisms (spirochete and fusiform bacilli).

A mixture of arsenic and ipecac, as recommended in a previous paper, was used three times daily as an application to the gums and lips, and also as a mouth wash. Boracic compresses were advised for the eyes. In twenty-four hours the mouth felt "easier," although it was impossible to open the lips. Three days later the patient admitted that he had a peculiar sore on the penis, and this on examination was found to be a small red ulcer with a membrane over it surrounding the meatus. Smears showed Vincent's organisms present in large numbers. For treatment, the same solution as that used in the mouth was applied on a small pad of absorbent cotton, and changed three or four times a day. The ulcerated area was completely healed within a week. The Wassermann reaction was negative on two occa-

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sions. During the second week after admission the patient developed a severe pleuritis, with a fairly large amount of fluid present; but this apparently was simply coincident, and had no relation to the other conditions described here, although the chill and cough, which developed early in the disease, were the first signs of pleuritis.

When last seen the mouth, eyes, and penis were entirely healed, and the marked depression which was present at first had disappeared. This was one month after his admission to the hospital.

The primary infection was probably in the mouth and had been transferred to the glans penis and conjunctivae by means of the fingers. Treatment with the following prescription as a mouth wash, with directions that the mixture should not be swallowed, quickly cleared up the condition:

℞ Vin. ipecacuanhae 15
Glycerini 4
Liq. arsenicalis 15

Pyoderma Resulting from Scabies and Pediculosis. Some interesting observations on the dermatoses encountered in a military hospital have been made by Semon and Barber[5] of the British army.

Scabies and pediculosis are the most common disorders in their service and almost never occur without severe secondary infection. A patient with scabies frequently shows cutis anserina, or "goose flesh," due to the erection of the pilo-sebaceous follicle. Another interesting fact is that *Acarus scabiei* is a potent factor in causing an exacerbation of seborrhoic dermatitis, which is made still worse by the sulphur treatment.

Pediculus vestimentorum is commonly supposed to deposit the eggs only in the clothing, but the writers were able to find the ova deposited on the hair of the pubic region, and when these ova were incubated the pediculi were identified as *Pediculus vestimentorum*.

The chief points in the differential diagnosis of the lesions due to scabies and pediculosis are tabulated as follows:

(5) Brit. Jour. Dermat., Vol. 29, p. 173.

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LOCALIZATION.

Scabies.	*Pediculosis.*
Head, wrists, elbows, anterior axillary folds, umbilicus and abdomen, lower buttocks, penis, and about knees.	Posterior axillary folds, shoulder, sacral region, upper buttocks, groins, thighs, and skin between knees and ankles.

TYPES OF LESIONS.

Scabies.	*Pediculosis.*
Burrows, vesicles, small superficial crusts, papules and cutis anserina. Scratch marks are represented by minute blood crusts at apices of the erected follicles.	Superficial and deep pustules with a surrounding red and indurated halo. Circular encrusted ulcers of varying depth and size but much larger as a rule than in scabies. "Linear impetigo."

The best prophylactic for pediculosis is the solution of naphthalene 1 per cent. and sulphur 1 per cent. in benzol or petrol first recommended by Captain Gunn. This is lethal to both parasites and ova.

A Peculiar "Blue-Spot" Eruption in Soldiers. Four cases of a peculiar "blue-spot" eruption have been observed by Lawrence and Trewhella[6] in a base hospital in England.

The patients were soldiers, sent to the isolation ward as suspects of cerebrospinal meningitis. On admission there was, in each case, an elevation of temperature, varying from 101° F. to 103° F.; this fever period lasted for from three to four days. After the temperature became normal the patients felt comparatively well.

From two of the patients meningococci were obtained from the throat; but none of them developed symptoms of cerebrospinal meningitis. Captain Trewhella said the throats of all four patients showed the clinical appearances as met with in the throats of abortive cerebrospinal meningitis. In no case was the eruption present when the patient was admitted. Trewhella is quite certain upon this point, as he examined each patient carefully when admitted for any evidence of a cerebrospinal men-

(6) Med. Jour. Australia, March, 1917.

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ingitis rash. The rash appeared on the second or third day after admission.

The eruption consisted of macules of a slate blue or steel gray color, and not palpable, giving rather the appearance of a depression in the skin. The macules varied in size from that of a split pea over the abdomen to that of a sixpenny piece on the lumbar regions and the back of the thighs.

The eruption appeared upon the abdomen and sides of the chest, small of the back, the buttocks, back and front of the thighs. It was not accompanied by any symptoms. It appeared quickly over the parts mentioned and only a few spots developed later elsewhere.

The spots did not disappear upon pressure, although they did not become more evident under pressure with convex glass, as is the case of purpuric spots. The spots remained the same color for three or four weeks and then very gradually disappeared, some being still noticeable up to the seventh or eighth week.

The spots had the appearance of the rash known as *tache bleuâtre*, which is attributed to the action of pediculi, *pediculus pubis* in particular. In fact, the rash was so like *tache bleuâtre* that a colored plate depicting this eruption in Murchison's "Continued Fevers" (1884) could well be used to illustrate any one of these cases.

Captain A. V. Anderson, senior physician to the base hospital, who saw three of these cases, said he had seen similar spots in cases of typhoid fever, and had reported his cases as *taches bleuâtres* in the *Australian Medical Journal* of 1894. Other writers report *taches bleuâtres* occurring in typhoid, and no doubt the reason this condition has been noticed in particular in typhoid is on account of the careful search made for the usual rash occurring in this disease. Jacobi says *taches bleuâtres* soon disappear spontaneously.

Osler says that he had never failed to find some evidence of pediculi in all cases of *tache bleuâtre* that had come under his observation. *Tache bleuâtre* has been produced experimentally by crushing up specimens of *pediculus pubis* and inoculating them into the skin with a lancet, showing that some poisonous substance in these

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parasites has the effect of producing this peculiar blue-spot coloration of the skin. However, Captain Trewhella and the author are quite sure that no pediculus was present in any of these cases.

Properties of Tetryl. The symptoms produced in munition workers by Tetryl, and the methods for prevention of these disturbances, have been carefully studied by Cripps.[7]

The harmful effect of the nitro groups in the benzene ring is roughly proportioned to their number. The *chloro-nitro* compounds are even more dangerous, leading to the supposition that the toxic action depends on the negative or acidic character of the aryl body concerned. Tetryl is made by nitrating methyl anilin in the usual manner. It is met with in ground powder, fine and coarse, crystals and granular masses. As the size of the particles increases, the diffusion of the drug in the air diminishes. Hence workers object to working with the powder (see Plate V).

Workers having moist skins are more affected by tetryl than those with dry skins because of the fact that alkaline sweat is a good solvent. The skin lesion produced appears to be a traumatic inflammation, due to the powder getting into the clothing, setting up an inflammation which is increased by friction of the clothing. Marked loss of hair also occurs, probably due to the destructive effect of tetryl on the fatty substances in the sebaceous secretions.

The systemic disturbances consist of abdominal pains, respiratory difficulties (asthmatic and asphyxial), mucous membrane hemorrhages, headache and giddiness.

Methods of prevention consist of rejection of applicants who show evidence of dermatitis or eczema, pulmonary or gastric disorders and hyperidrosis; prevention of the powder gaining access to the body by ingestion, inhalation or absorption through the skin; washing of the exposed surfaces with ammonia water and change of clothing when leaving the factory.

Scarlatiniforme Erythema, Due to Ingestion of Melinite. An interesting case of subicterus and scarlatiniforme erythema, due to the ingestion of melinite for

(7) Brit. Jour. Derm., January, 1917.

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the purpose of escaping military service, is reported by Hollands and Fuchs.[8] The patient was a metallurgist 19 years old who presented a mild pharyngitis and an erythema over the trunk and arms, except the hands. The legs were not affected. The eruption was made up of small, yellowish vesicles around which there was a red areola. The lesions were very numerous and coalesced in places to form patches. The lesions developed without prodromes. The general health was not affected. The urine was of a grenadine red and contained a small amount of serum albumin, but lacked bile pigments. Examination of the urine showed the presence of picramic acid. The blood serum showed an orange-brown color due to the presence of the same acid. It also lacked bile pigments. The patient admitted having taken a yellowish powder, but insisted that it was for a blennorrhagia. This yellowish powder was found to be melinite, and as soon as the powder was withdrawn all the symptoms disappeared.

Dermatitis Due to Explosives Used in Air Raids. J. H. Sequeira[9] calls attention to a form of dermatitis caused by the handling of powder from high explosive bombs and aerial torpedoes used in the air raid on London on June 13, 1917. Many bombs had been dropped in various parts of the country on previous occasions, but there had been no dermatitis of this particular type. It is evident that some new substance is being used.

Sequeira has now seen fifty-nine cases of dermatitis, in thirty-five males and twenty-four females, and they fall into two groups. The majority, following the raid of June 13, first attended the London Hospital during the week ending June 30, with a few stragglers in the next week. The later group, due to the July 7 raid, began to attend for dermatitis on and after July 18.

The clinical picture is distinct. The initial staining is nearly always of a distinct orange tint. It is especially well seen on the palms. After the lapse of nine days (as a rule), the patients complain of intense irritation and itching, which interferes with sleep. This is followed by the appearance of closely set, discrete vesicles

(8) Lyon méd., October, 1916.
(9) Brit. Med. Jour., Aug. 4, 1917.

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the size of hemp seeds. These are on the palms and along the sides of the fingers and in the interdigital clefts. The backs of the hands are swollen, and there are occasionally small vesicles the size of millet seeds. There is not much redness of the parts. The eruption of the vesicles increases, and in many cases huge confluent blebs form, some of which are as large as a hen's egg. From one bleb, 20 c.cm. of clear serous fluid was obtained, and in another instance the fluid dripped copiously from a ruptured vesicle. On the feet, the phenomena are similar but the vesicles are rarely larger than a pea. In a few instances the lesions rapidly became infected and pustules formed, and in another a widely spread erythema with purpura on the lower limbs occurred. The eruption is at its height about the fourth or fifth day, and the epidermis gradually separates, leaving a raw, rather dry, red surface. In some cases seen early the vesicles dried up with desquamation. In a few instances the feet were affected after the hands, probably by contact. Occasionally the face has been involved, and in one instance a widely spread eczematous eruption formed. Most of the patients were in a nervous condition when first seen, while in others this symptom developed later from loss of sleep. In a few instances relapses are continuing, but are not so severe as the primary attack. Patients who wore gloves to clean up their houses suffered most severely.

Three patients were admitted to the ward on account of the severity of the symptoms. One case ran an apyretic course; in two others the temperature reached 100° F. on two evenings.

Dr. Panton found eosinophilia in three cases examined. In one instance 11 per cent. of eosinophiles were found, and in another 6 per cent. This was to be expected, and compares with Dr. Panton's report on trinitrotoluene cases.

As a prophylactic measure, it is important to avoid touching the powder or materials impregnated with powder. Its removal can be effected by moistening a surface with a weak alkaline solution (one teaspoonful of sodium bicarbonate to a quart of water). Brushes may be moistened with this solution. If the circum-

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stances permit, a hose may be used to wash down an apartment or surface covered with the powder. It is better not to wear gloves, as they soon become impregnated with the powder, and moist perspiring surfaces appear to be more easily irritated. Rags wet with the alkaline solution may be used.

If the skin of the hands be stained, an endeavor may be made to remove as much of the stain as possible by pumice, and by washing with the alkaline solution.

When the eruption has developed, the parts should be washed as little as possible, but the alkaline solution may be used without risk. The best local application is liniment of calamine (calamine 70 grains, lime water 1 oz., olive oil 1 oz.). This rarely fails to allay irritation and to promote healing. If the parts become septic, the usual remedies are of service, and in a very bad case spraying the parts daily with a malachite-green sublimate solution was of great value. The solution, which we owe to McIntosh and Fildes, is made as follows: Malachite green 1 part, hydrargyrum perchloridi 0.5 part, spiritus vini rectificati 100 parts.

The substance which is the cause of the dermatitis appears to be hexa-nitro-diphenyl-amine. The phenomena are identical with those caused by aurantia, an orange dye (ammonium hexa-nitro-phenyl-amine) which has been used for the dyeing of cheap brown shoes and other leather articles. In Prosser White's "Occupational Diseases of the Skin," p. 99, "aurantia, emperor's yellow," is described as "a basic aniline azo dye," which causes an abundant uniform-sized crop of vesicles, thickly crowded together all over the palm. Cases were recorded by Radcliffe Crocker, whose description of the phenomena of aurantia dermatitis on p. 417 of his textbook on "Diseases of the Skin" (third edition), tallies exactly with the appearance and symptoms which have been observed in the cases now described.

The use of the substance was prohibited in Germany, and it is not now used on either silk or wool in this country. In Thorp's "Dictionary of Applied Chemistry," vol. i, p. 340, it is stated that, according to Gnehm (Ber., pp. 1246, 1557) and Bayer and Co. (W.

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J. 1877, 879), aurantia produces skin eruptions. Martius contends that this effect is due to idiosyncrasy, and quotes the opinion of Salkowski and Ziureck in support of his statement. The ministerial order of Nov. 8, 1877, prohibiting its manufacture was cancelled in June, 1880.

Hexa-nitro-diphenyl-amine is recognized as an explosive substance, and is combined with trinitrotoluene in the bombs which have been used in the recent air raids in Great Britain.

Military Methods of Treatment.

Treatment of Scabies by Chlorine Gas. While carrying out the training of troops in the use of anti-gas measures involving exposure of the men to chlorine gas, the officer commanding one of the battalions found that the gas had cleared the camp of scabies. This led Captain Clark and Captain Raper of the Royal Army Medical Corps[1] to make an investigation of the value of chlorine in scabies and to determine the optimum concentration of the gas.

About sixty cases of scabies in non-commissioned officers and men and fourteen cases in officers were treated by exposure to chlorine. The details of the treatment differed in the two cases.

The non-commissioned officers and men were exposed to a concentration of one to two parts of chlorine per thousand of air (by volume), the service gas helmet being worn as a protection. The exposures were of five minutes duration and occurred on successive days. Usually four exposures were given, but in some instances this number was exceeded.

The patients had a hot bath before their first treatment and wore ordinary hospital clothing. At the first exposure the bedding was placed in the "gassing" chamber. The officers wore a box respirator as protector, and were exposed to a concentration of between two and three parts of chlorine per thousand of air. The exposure lasted twenty minutes. A bath was taken on the morning of the first day of treatment and not

(1) Brit. Med. Jour., July 28, 1917.

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again, except in one case, until the day after the last exposure of gas. The number of exposures given and the intervals between them were varied in order to find out the best conditions of treatment.

A few of the men were given four exposures on successive days, and then, after two days' interval, two more exposures on successive days. Others received two exposures on the first two days, then, after two days' interval, two further exposures on successive days. Three of the officers were given two exposures on the first two days, and then, after three days' interval, one more exposure only. On the first day of treatment the officers' underclothing, sleeping garments and gloves were exposed to the gas, and clean bed linen was ordered the same night. The clothing was exposed for twenty minutes. The treatment of both officers and men was carried out in rooms with about a thousand cubic feet of air space. Chlorine was delivered into this from a cylinder, and it was found, after very little practice, that an approximation to the concentration desired could easily be obtained. The concentration in all cases was determined more exactly by drawing with a siphon a measured volume of the air through 5 per cent. sodium iodide solution and titrating the iodine liberated with sodium thiosulphate.

If 1,100 c.cm. of air are drawn through the iodide solution, and decinormal sodium thiosulphate be used in the titration, then each cubic centimetre of thiosulphate used is equal to one volume of chlorine per 1,000 volumes of air.

The point of the delivery tube of the burette was pushed through the cork of the wash bottle containing the sodium iodide, so that the titration could be carried out in the gas chamber. If the iodine be not overtitrated, then several determinations of the concentration can be made by refilling the siphon bottle and again drawing through the wash bottle a known volume of air.

Nearly sixty non-commissioned officers and men were treated under somewhat unsatisfactory conditions at a military hospital in the London district with the method of treatment as described above. Of the whole number

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PLATE V.

Eruptions due to contact with tetryl. The first three women were pellet makers; the fourth woman was a gauger.—Cripps (see page 83).

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the medical officer of the hospital reported not more than 25 per cent. as cured. Many of the patients not definitely cured showed much improvement.

The comparative failure of the treatment of the non-commissioned officers and men may be ascribed to the exposure to chlorine being of too short a duration, and also to the fact that the concentration of the gas used was on the average not more than one per thousand of air.

Of the fourteen officers treated, eleven were cured and three much improved. Eleven of the officers received four or more exposures, and of these nine were cured. The two who still had apparently active lesions had received six exposures. Two officers were given four exposures on six days, the two middle days forming an interval. Both were cured; one, however, was a mild case. Three officers received three exposures only, one on each of the first two days, and the third on the sixth day. Of these two were cured, and the third was almost free of scabies a week after the last exposure.

These figures make it appear that usually four exposures are sufficient when given on the first, second, fifth and sixth days.

One feature of the treatment which was noted in officers, non-commissioned officers and men was the production of a very irritable condition of the skin, especially about the scrotum and axillae, in some of the cases. It was most marked in cases which may be termed chronic, and which the men had been treated by sulphur in one form or another for varying periods without cure, and also more noticeable in the cases which were given more than four exposures. The authors have noted the same condition in themselves while working in chlorine gas for various purposes. It passes away completely as a rule in the course of one or two weeks and is relieved to some extent by adding a little washing soda to the daily bath.

It is only possible to surmise as to the active agent in the cure. The toxic properties of chlorine are well known, and no doubt the acarus is affected by the gas diffusing into the burrows.

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Numerous cases of scabies were occurring in a mounted section which was sleeping in temporary barracks. They were all passed through a considerable concentration of gas in a state of nudity, helmets being fastened round their necks with towels. The gassing was carried out in their sleeping quarters, all their clothes and bedding being treated at the same time. The medical officer reported that no further case of scabies occurred for more than two months thereafter.

[In our experience from three to five daily applications of 15 per cent. sulphur ointment will cure every case of scabies. Reinfection, of course, will occur unless all the clothing be sterilized.—EDITORS.]

Treatment of Scabies by Sulphur Fumigation. The necessity for treating a large number of soldiers for scabies led Lieut. Col. Bruce,[2] R. A. M. C., to try the effect of sulphur dioxide.

The treatment consists in exposure of the patient to the fumes of a sulphur candle for forty minutes in an improvised vapor bath cabinet. As sulphur dioxide acts more efficiently in the presence of moisture the interior of the cabinet is heated artificially, if need be, to promote perspiration. One application is sufficient. All of the patient's belongings must be sterilized with steam or formaldehyde at the same time.

Coal Tar in Military Dermatology. The use of coal tar as a therapeutic agent has been frequently referred to in these volumes.[3] Captain Semon,[4] R. A. M. C., records his experiences with a combination of equal parts of pix carbonis B. P. acetone and flexible collodiom. The only apparatus required is a house painter's brush. No other dressings are required, and hence much time and material are saved in a base hospital. It was found of great value in seborrhoeic dermatitis, psoriasis, vesicular eczema, and lichenification, but under no circumstances should it be applied to an infected surface.

(2) Brit. Jour. Derm., 1917, p. 83.
(3) Practical Medicine Series, 1915, Vol. IX, p. 123.
(4) Brit. Jour. Derm., 1917, p. 100.

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TREATMENT OF DERMATOSES.

Intravenous Injection of a Foreign Protein for Dermatoses. It is a common experience to observe beneficial effects in certain skin lesions from intercurrent infections associated with high temperature. The nodules of leprosy sometimes rapidly disappear after an intercurrent infection associated with high temperature; the bite of a cobra, as is well known, frequently causes a rapid resolution of the cutaneous lesions in this disease. Psoriasis may disappear during an intercurrent pneumonia, or typhoid; likewise the lesions of mycosis fungoides may improve temporarily after an intercurrent infection. This has been artificially produced by M. F. Engman and R. A. McGarry[1] in two cases by the injection of Coley's fiuid (probably owing to the foreign protein). In one case the disintegration was so rapid that it caused an earlier dissolution of the patient than would otherwise have occurred. A similar retrogression of lesions during hyperpyrexia has been observed in syphilis, and tuberculin has been known to affect the efflorescence on the skin after a "test" injection.

Interest in the artificial production of high temperature as an experimental method of treatment for various diseases of the skin has been renewed in an article by Jobling and Petersen in which they discuss the subject of specific therapy in its relation to the production of certain changes in disease. From their investigations made at former times, they came to the conclusion that it seems probable that the remedial effects apparently produced under such conditions are due to "colloidal dispersion, in that the injections probably bring about a less dispersed state, affecting not only the serum proteins but also the serum lipoids."

In other words, Jobling and Peterson believe that the beneficial effects produced in typhoid and in other diseases by the injection or accidental introduction of foreign proteins are due to the mobilization of ferments, as "in experimental animals the intravenous injection

(1) Jour. Amer. Med. Ass'n., Dec. 9, 1916.

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of bacteria, kaolin, protein-split products and trypsin is almost invariably followed by more or less marked mobilization of serum protease and usually of lipase." They state that in the patient a similar reaction occurs following the intravenous injection of vaccines and proteoses, but not to the same degree or with the same regularity as in animals.

Miller and Lusk report the startling influence on typhoid fever by the injection of the proteose as prepared by Jobling and Petersen, and state that they obtained the same result with this agent in the abortion of typhoid fever as they did with the intravenous injections of typhoid vaccines. Their results were simply confirmatory of those already recorded by other observers, but they believe that the apparent sudden termination of the disease was probably not due to the specific action of the typhoid vaccine, as proved by these investigations, but to the introduction of a foreign protein. They, therefore, decided to apply the method to acute, subacute and chronic arthritis. The results in these conditions were equally startling and satisfactory.

Louis D. Smith has found that the virtue of the antigonococcus serum in gonorrheal patients is due not to its specific effect, but to the anaphylaxis produced in the patient by the horse serum. His results were equally clinically striking and beneficial, owing, no doubt, to the introduction of a foreign protein and not to the anaphylaxis.

These results encouraged Engman and McGarry to experiment with some foreign protein in the treatment of various skin diseases. To carry on these investigations they decided on a typhoid vaccine as prepared by one of the reliable manufacturers as the most convenient for their use and one that could be obtained without a great deal of laboratory preparation.

The patients were taken at random as they entered the hospital, and those selected in which the etiologic origin was more shrouded in mystery or due to a known microörganism. All the patients were kept in the hospital through the course of treatment and under close observation by the house-staff. Except with one patient, all the injections were intravenous, varying from 75,000,000

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PLATE VI.

Rupioid psoriasis before and after auto-serum treatment. (See editorial comment page 93).
(Case in photographic series of Ormsby and Mitchell.)

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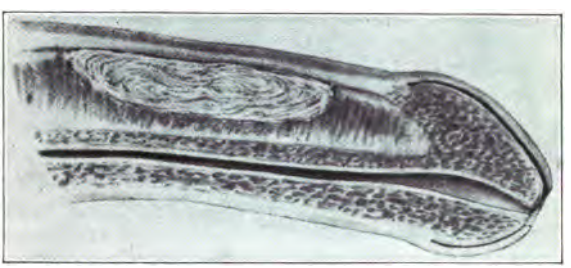
PLATE VII.



Showing indurated mass in penis.—Hertzler (see page 108).

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to 500,000,000 of the so-called "prophylactic" suspension of the typhoid bacillus.

In none of the cases was there any lasting inconvenience noticed. All the patients had chills accompanied by a sharp rise in temperature from 100 to 105° F. All showed a slight, but not marked rise in the number of leukocytes. In one case, after the second injection, a marked nephritis with some microscopic blood in the urine developed, but the patient quickly recovered under rest and a selected diet. In all, the local lesions, especially in lupus erythematosus, became much redder and sometimes itched and burned for from an hour to three hours after the injection. Herpes labialis was a common occurrence after the chills and fever.

Five patients with psoriasis were given this treatment, of whom two seemed to be slightly, if at all, benefited. It was found, however, that on the first or second day after the injection there is a marked blanching of the lesions, less scaling, and a slight disappearance of the infiltration; and even in the resistant cases, dark pigment stains can be seen where certain plaques have disappeared. However, in the most favorable cases, unfortunately, relapse has occurred within a short time.

A group of patients with lupus erythematous treated in this manner showed marked improvement. The reactions, however, were sharp and necessitated hospitalization. Recurrence was frequently observed shortly after treatment.

[In our hands auto-serum therapy (*Vide* Practical Medicine Series, Vol. IX, 1915) has caused the temporary disappearance of the lesions in a large number of psoriatics. Injection of foreign protein appears to accomplish nothing more than that, and it has the disadvantage of giving a sharp and even dangerous reaction. (See Plate VI.)—EDITORS.]

Non-Specific Protein Treatment of Psoriasis. In a recent communication, Schamberg and Raiziss[2] have reiterated and corroborated the conclusions voiced in two former papers, namely, that the nitrogenous metabolism in psoriasis presents considerable deviation from that of normal individuals.

(2) Pages 5-8, this volume.

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These experiments of Schamberg and his coworkers are of great interest and fundamental importance as they point to a metabolic error that must be corrected by a constitutional agent or influence that will stimulate the body cells to deal normally with the protein intake. Low protein diet may be of service in relieving the condition, as it brings to the functionally damaged cells a smaller amount of a material which they are incapable of metabolizing in normal fashion, and so less imperfectly metabolized nitrogen can accumulate in the organism.

The normal organism rapidly adjusts itself to the nitrogen level in the food supply and continues in equilibrium, whereas the psoriasis patient, as shown by Schamberg, stores nitrogen even on a low nitrogen intake. Chittenden and his coworkers have shown that nitrogen equilibrium may be maintained at a lower level than was used by Schamberg, so there can scarcely be question that the psoriasis patient has a faulty mechanism for dealing with protein, and this is not a difficulty in absorbing the nitrogen, but is apparently a fault of cellular metabolism. The favorable results obtained by Walker in giving psoriasis patients thyroid extract may be due to the well-known stimulation to metabolism which this gland extract produces.

The therapeutic method described by Van Alstyne[8] approaches the matter from another angle. It has been demonstrated by so many investigators that particular reference is unnecessary that parenteral injection of a foreign protein stimulates the development of enzymes capable of splitting the particular antigen much as the digestive enzymes pepsin and trypsin do. There is, furthermore, much evidence that an antigen stimulates antibodies not in all respects specific. Certain of the methods used in experimental work show that some of the reactions produced by foreign protein injection are specific to a high degree, notably the anaphylactic reaction; others seem to be class reactions, and Hektoen has shown that the antibodies developed from bacterial proteins have class reactions. Clinical observations afford some substantiation of such ideas. It seemed possible to stim-

(8) Med. Record, Sept. 29, 1917.

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ulate the capacity of the organism to deal with protein more effectively by giving subcutaneously injections of a comparatively non-toxic foreign protein. Such a method has been followed in the treatment of the author's cases of psoriasis, and while it is not possible as yet to give figures to show whether such treatment corrects the nitrogen retention, the clinical results are so striking, he thinks, as to warrant their publication.

The protein selected for this purpose was prepared from the millet and alfalfa seed by the method recently described by Bebbe and Williams.[4] The method in question is a simple one:

"Fifty grams of the seed meal are placed in a flask with a reflux condenser; 1,000 c.c. of distilled water and 40 c.c. of 10 per cent. hydrochloric acid are added. The mixture is boiled for three hours and the coarser particles strained out through gauze. The filtrate is concentrated to 200 c.c. approximately and the excess of acid neutralized with 10 per cent. solution of sodium hydroxide. It will be found that an abundant precipitate of acid albumin forms when the extract is neutral to litmus. It is best to add sufficient sodium hydroxid to get a very faint alkaline reaction to litmus. A portion of the first precipitate formed will redissolve under these circumstances. The faintly alkaline solution is filtered, the filtrate concentrated to such a point that its nitrogen content is 0.3 per cent. as measured by a Kjeldahl determination. The concentration needed for this purpose varies somewhat in each case, but the final bulk of the standardized protein solution from this amount of material is about 100 c.c. If the reaction be very faintly alkaline the solution may readily be sterilized by boiling. The solution contains alkaline albumin, proteoses, and a small quantity of peptone. It is a most excellent culture medium for a variety of organisms and ought to find extensive use in bacteriologic laboratories, but for therapeutic use the only safe way to preserve it is to seal the solution in small glass ampoules which are then sterilized by the discontinuous method."

Such proteins have been given to a great many

(4) Med. Record, Vol. 92, No. 3, p. 98.

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patients in doses of from 6 to 20 minims without any disturbing reaction. None of the cases treated were in a hospital nor did the injections in any way interfere with their usual activities. The injections have been given subcutaneously in the upper arm midway between the elbow and the shoulder. The reaction is so slight as to be negligible. In one instance there was a local erythema with some heat and swelling, but this occurred only after a single injection in one patient.

Four cases of psoriasis were treated by this method. The improvement in the skin lesions begins in from two to five weeks after the injections are begun, at a time when the larger injections have been reached. The skin lesions improved without modifying the diet and without the use of local applications.

It is not possible to make any predictions as to the permanency of relief afforded by this method. It seems possible, however, that when a good condition of the patient is once established, an occasional injection may be serviceable in preventing an exacerbation. The injections in no way interfere with the dietary or other forms of treatment that have been used in the past with reported good results. Possibly in stubborn cases a combination of these measures with protein injections may produce more prompt results.

Sulphur Injections for Psoriasis. In 1907 Bory first suggested the injection of colloidal sulphur. At that time he used glycerin as a base, but this was found to be very painful when injected intramuscularly.

Bory[5] is now satisfied that he has found a formula answering all the requirements for intramuscular injections. The formula is as follows:

℞ Sulphuris ppt. 20
Eucalyptolis 20
Olei sesami 80

The oil of sesame should be warmed and the sulphur rubbed up in it until dissolved. The solution is then cooled, after which the eucalyptol is added. The resulting liquid is an oily solution of sulphur containing 2 mg. per cubic centimeter. Five cubic centimeters are in-

(5) Presse Méd., June, 1917, p. 331.

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jected intramuscularly every three or four days. Locally, Bory applied a 25 per cent. solution of eucalyptol in collodion.

A small number of cases were treated very successfully. Some of the inveterate cases showed marked improvement after two or three injections, but as many as fifty injections were necessary in one case before the lesions cleared.

Treatment of Yaws by Salvarsan and Allied Remedies. In the statement by Raoul de Boissiere,[6] district medical officer, Fiji, are embodied the results of extensive observations in the treatment of yaws, and more especially those obtained by the use of one or another of the "salvarsan" products during a period of twelve months, ending Dec. 31, 1916. The remedies used included novarsenobenzol-billon, arsenobenzol-billon and kharsivan. A total of 182 cases were treated, consisting of 107 males and seventy-five females. With the exception of one half-caste patient from Aquara Island, the patients were Fijians.

The ages of the patients ranged from 4 months to about 65 years. The cases of "coko" or secondary yaws all occurred among children under 7 years of age, mostly among those between 1 and 3 years old. There was one solitary exception—that of a boy of about 12 years of age, who was suffering from well-marked and extensive condylomata about the anus and scrotal regions. No less than eight of the thirty cases showed well-defined and extensive condylomata about these areas, resembling exactly similar lesions seen in Europe among patients suffering from syphilis.

The duration of these affections was given as being from four months in a few cases to thirty-five years and more, the latter cases being in certain old men who claimed to have suffered from "soki" since youth. Many of these men for years had been incapacitated for much walking on account of the great pain produced by the soki on the soles of the feet.

The drugs were given intramuscularly in aqueous solution. No complication was noted in any of the cases injected, not even an abscess was seen. The doses were

(6) Edinburgh Med. Jour., October, 1917.

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extremely well-borne by young and old. The intramuscular injections of arsenobenzol-billon and kharsivan always caused considerable pain at the time. The injection of the novarsenobenzol-billon was much less painful than the other preparation.

The majority of patients required only a single dose to effect the complete disappearance of the lesions complained of—180 out of 182 cases. In a considerable number of cases, however, recurrence of the trouble was subsequently noted, more especially among those patients treated with novarsenobenzol.

The following table is of interest:

Drug Used.	Number Treated.	Number of Relapses.	Percentage of Relapses.
Novarsenobenzol	44	7	15.99
Arsenobenzol	49	0	Nil.
Kharsivan	89	2	2.24
Totals	182	9	4.94

In five of the above 9 patients who relapsed, a dose of arsenobenzol of kharsivan was subsequently given with the happiest results.

[Many workers are of the opinion that salvarsan is more efficient than neosalvarsan in syphilis, but as yet there appears to have been no attempt to determine this point by treating a large series of cases. A comparison of the results of the two drugs in yaws points to the greater efficiency of salvarsan.—EDITORS.]

Lumbar Puncture in Lichen Planus. The relief of itching in lichen planus by lumbar puncture was first noted by Pernet. At that time he reported the interesting observation that the spinal fluid of such patients was normal in all respects save one, namely, the failure to reduce Fehling's solution. The patient had received biniodide of mercury for some time by mouth.

In order to determine what rôle the previous treatment had played in the failure of reduction, Pernet[7] examined the fluid of a patient who had received no treatment. In this case the fluid showed the normal reducing power. Halliburton says that this reduction

(7) Ann. derm. et syph., September, 1916.

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is due to the presence of glucose and that after standing for a few days the fluid loses this reducing power owing to the presence of a glycolytic ferment elaborated by the pituitary gland.

Treatment of Tinea Versicolor with Adhesive Plaster. Stanley,[8] in the course of a routine examination of a newly admitted prisoner in San Quentin prison, observed that there were bands of normal skin through areas of tinea versicolor. Questioning of the prisoner elicited the fact that he had had adhesive plaster applied nine months previously for a dislocated shoulder.

In order to prove the curative power of adhesive plaster in this condition, strips of ordinary plaster were placed over areas where the tinea was thickest. These strips were left on twenty-four hours and forty-eight hours respectively. On removing the first one, the skin appeared to be normal and some of the brownish discoloration remained on the plaster. A few patches subsequently reappeared in this area.

The second strip applied for forty-eight hours permanently cured the disease over the area on which it was applied.

To one area where it was impracticable to apply the adhesive strips, a 12 per cent. solution of sodium hyposulphite was applied several nights in succession. This succeeded in curing the disease.

[We have found the Whitfield ointment, consisting of 6 per cent. salicylic and 12 per cent. benzoic acids, used in the treatment of ringworm of the feet, to be very effective in the treatment of tinea versicolor.—EDITORS.]

Treatment of Localized Hyperidrosis. Circumscribed hyperidrosis is a common disorder of the skin which may usually be classed among the petty annoyances of life. Not infrequently, however, especially when complicated by bromidrosis, dysidrosis or hyperkeratosis, it assumes a much more important rôle, incapacitating the person for work or pleasure. Walking is made so painful as to be impossible; the use of the hands is similarly interrupted; or the knowledge that an unpleas-

(8) California State Jour. Med., August, 1917.

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ant odor clings to one makes the sensitive person dread to meet others.

Treatment has always been unsatisfactory, as evidenced by the list of remedies recommended, until the discovery that Roentgen rays would control it. The latter treatment, however, is time consuming and expensive, and not without danger in inexperienced hands. An efficient and inexpensive local application is much to be preferred.

Stillians[1] treats the condition as follows:

A 25 per cent. solution of aluminum chloride in distilled water is dabbed gently on the part every second or third day and allowed to dry on. This will cause a rapid amelioration of the excessive sweating. It is usually sufficient to make three such applications, then to wait for a recurrence before resuming treatment; or one application a week may be made to ward off recurrences. Dress shields, which aggravate the trouble by their impenetrability, can often be discarded after a few applications.

The drug is not wholly bland, for excessive use of it will cause a sharp itching or stinging sensation which usually subsides spontaneously if the part be not scratched. Excessive or careless use followed by scratching can easily cause a dermatitis, but this rarely happens when reasonable care is exercised. To avoid it, the patient should be instructed to allow the lotion to dry thoroughly before clothing is permitted to touch the skin, and should be warned against excessive use. If itching does occur in spite of precautions, an ointment of cold cream containing 12 per cent. boric acid may be used, or a calamine lotion with or without 0.5 per cent. phenol (carbolic acid).

In twenty cases in which Stillians used this lotion, it has never failed to give relief. Most of these were cases of simple local hyperidrosis of the axillae or feet; but three were cases of persistent vesicular eruption of the feet accompanied by excessive sweating.

Fissure of the Lip; a Device for Its Treatment. A fissure in the midline of the lip is a great annoyance to the patient and a trial of the skill of the dermatologist.

(1) Jour. Amer. Med. Ass'n., Dec. 30, 1916.

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A simple method of treatment had been used with good results by Pusey.[2]

The reason that fissures are rebellious to treatment, of course, is that they are kept open—as they are formed —by the movements of the lips. To heal them promptly, it is only necessary to apply a fixed dressing to prevent this splitting, and the device suggested is the application of a piece of adhesive plaster on the vermilion border of the lip across the fissure, so that it will prevent the spreading of the lip at the fissure. Such an adhesive plaster dressing, if well applied, will adhere for from twelve to twenty-four hours. It then becomes loosened by the saliva. The patient should be instructed to apply immediately a new strip when the old one becomes thoroughly loosened. For the same purpose Pusey formerly used a little dressing of gauze and collodion, but the adhesive plaster is easier to apply and adheres longer.

It is surprising how much relief this dressing gives; with it the individual can talk, laugh, cough, sneeze or eat without the inevitable cracking of the lip. The application of such a dressing for even twelve to twenty-four hours will allow most to heal sufficiently to be able to withstand the movements of the lips, and so go on to complete healing without further dressing. A few days' application of such a dressing will cure the most persistent fissure.

[We have had good results with radiotherapy in fissures of long duration.—EDITORS.]

Treatment of Chancroid. Regardless of the appearance, duration or previous treatment of a venereal sore, before it be destroyed it should always be examined repeatedly for spirochetes. If the examination prove negative Robbins and Seabury[3] treat the ulcer in the following way:

A 25 per cent. solution of copper sulphate in distilled water is applied to the sore, and the short high-frequency spark from a rather fine-pointed vacuum electrode is applied directly to the sore for from one to three minutes, depending on the extent of the ulceration. Especial care is exercised in carrying the point

(2) Jour. Cut. Dis., January, 1917.
(3) Jour. Amer. Med. Ass'n., Oct. 13, 1917.

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of the electrode well down into any fissure or undermined edge, and the area of application should extend over the edge of the sore about one-sixteenth inch into the doubtfully healthy area.

The current is not turned off until every crack and crevice has been thoroughly treated and the surface of the sore is changed to a dark greenish gray. It is then wiped dry and some antiseptic powder is lightly applied to the entire mucous surface of the preputial cavity. If the sore be exposed, it should be covered with a thick moist dressing, for which any very dilute antiseptic may be used, as a 1:10,000 or 1:20,000 mercuric chloride solution; or even tap water answers nicely in most cases. This should be changed once or twice daily, and must not be allowed to stick.

The patient is instructed to return in two days, and, if the work has been carefully done, the wound will present a perfectly healthy granulation that will go on to complete healing in a few days. If the sore does not look clean, the application is repeated at the second visit. The patient returns each second day. If the original sore was large, or if a small sore does not seem to be closing rapidly, one should apply, at each visit, either a 10 per cent. copper sulphate or a 5 per cent. silver nitrate solution. There should be no hesitation in repeating the original cauterization at any time one has reason to think the chancroidal infection is not completely eliminated.

The success of this, as of any other method, is dependent on careful, thorough work. There is more danger of too little cauterization than of too much, and thorough cleansing at the time the sore is destroyed must not be forgotten. Again, the after-care, especially with ulcus molle outside the preputial cavity, and with ulcus molle miliare, is of the utmost importance. If one fail to carry the electrode to the bottom of the cavernous ulcer, failure may be the result; the surface may heal over and in two or three days break out anew, larger and deeper than before.

If the dressing on an exposed surface be not changed once daily, and moistened at least three or four times, in many cases one will not succeed.

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Treatment of Impetigo Contagiosa. The treatment of impetigo contagiosa with ammoniated mercury preparation has been found by Morrow[4] to be of little value. The use of silver nitrate he finds to give much better results.

The method is as follows: The vesicles or pustules are ruptured with gauze, the sodden epithelium which comprises part of the wall is removed, and the base of the lesion is thoroughly covered with a silver solution, the application of which is made with a swab. Where crusts have formed it is usually an indication that the disease is still spreading at the base. The crusts should likewise be removed by rough friction with gauze, and the underlying areas treated with a 20 per cent. silver solution applied in the same way as to the vesicular and pustular bases.

When other drugs are added to the silver nitrate solution, in order to avoid staining of the skin, the value of the remedy is lost. Likewise when the colloidal and complex silver salts are employed, the results are just as disappointing.

New lesions can usually be prevented by washing with boric acid solution, or with a weak solution of mercuric chloride. The patient should always be examined carefully and often, in order that new lesions may be recognized in their first stages and promptly aborted.

It is advisable to apply a dusting powder, preferably one containing ammoniated mercury in the strength of from 6 to 10 per cent. and boric acid powder up to from 15 to 20 per cent. When the impetigo is on an uncovered part, even without the silver, the powder form of treatment should be selected in preference to a grease. Such a powder should be applied after swabbing with silver solution, and by the patient several times daily. The most satisfying manner of applying the powder is by means of an insufflator. Adults who have the infection on the face should not shave until all active signs of it have disappeared and they should not subject themselves to the irritation of the wind, such as results from motoring in open cars. Needless to say, children suffering from impetigo should be restrained from at-

(4) Jour. Amer. Med. Ass'n., July 21, 1917.

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tending school until they are entirely well; and, furthermore, all prophylactic measures should be enforced to prevent others who occupy the same living quarters from acquiring the disease. New-born infants should be removed as soon and as completely as possible from victims of impetigo, for they seem not alone very susceptible to the infection but are often gravely affected by it. Since that form of impetigo which attacks the new-born differs as a rule widely from the variety of the malady encountered in early youth and in adults, it should receive its own special medical attention. Although small vesicles and small pustules, along with slight crust formation, may be observed in an impetigo eruption of the new-born, the disease usually tends toward the formation of bullae, which appear with great suddenness, and increase in dimension with almost incredible swiftness, occasionally reaching the size of an adult palm in a few days' time. In these cases ammoniated mercury ointment seldom checks the advancing borders, and instead of a cure being achieved, we frequently see the lesions progressing to the formation of enormous flaccid bullae. It is the rule for these bullae to rupture, their thin covering of epidermis sloughing away, leaving large denuded areas resembling superficial burns. The accumulation of sodden epithelium on the diseased skin surface, and of pus, crusts and of greasy detritus, leads to a general pathologic condition which all too often has a fatal ending. If these cases are recognized in the beginning, and the lesions aborted with silver, further dire results of the infection can usually be avoided. It is not infrequently necessary to apply the silver daily to certain portions of the border where the disease has not been stopped in its advance. Clothing produces heat and friction with infants, so it is advisable to keep those who have impetigo in a suitably warm room and with as few garments on as possible. With only a limited amount of material for forming this statement, exposure of these infants to the direct rays of the sun has seemed to be a distinct help in securing a cure. However, it must be emphasized that this form of heliotherapy should not go to the ex-

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tent of producing an erythema of the unaffected areas of the body.

[We find that impetigo yields promptly to the following method of treatment. The parts are bathed for from fifteen to twenty minutes night and morning in hot 1-2,000 mercuric chloride solution, after which at night a 10 per cent. ammoniated mercurial ointment is applied, and in the morning a 25 per cent. calomel powder is dusted on.—EDITORS.]

Electric Cautery in Cutaneous Surgery. There are many skin lesions that demand removal and Hazen[5] discusses the various means at our disposal. To remove such growths we have a number of methods. There are the various caustics, such as arsenic, zinc chloride, trichloracetic acid, the acid nitrate of mercury and caustic potash. Carbon-dioxide snow probably should be classified in this group. Among the electric methods there are fulguration, diathermy and the electric needle. The Roentgen ray and radium are used in some conditions and, lastly, there remain the curette, the knife and the cautery, either Paquelin or electric.

The caustics have certain marked disadvantages: the superficially acting ones, such as silver nitrate, are worthless except in some extremely superficial lesions, and the ones that act deeply are extremely difficult to control, especially as they must act over a considerable space of time. The pain is usually intense; any patient who has had an arsenic paste employed for cancer is not anxious to repeat the experience, unless he enjoy martyrdom. Carbon-dioxide snow obviates some of these disadvantages, for it is quick and usually not painful, but as a rule it does not act sufficiently deep. From considerable personal observation, the author does not believe that fulguration and diathermy present any value that the cautery can not equal, and in addition they are much slower in their action. The electric needle is of value in removing small, superficial, nonmalignant conditions, for it is painless and leaves an excellent cosmetic result, but it is entirely too slow for large lesions.

The field of the Roentgen ray and of radium is

(5) Jour. Cut. Dis., September, 1917.

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small, although at times they are of extreme value in handling cases of cancer, sarcoma, lupus vulgaris, blastomycosis, keloids and many of the inflammatory skin diseases.

The use of the curette alone is always to be deplored, inasmuch as it leaves an ugly, jagged wound, and inasmuch as it can not touch the outlying pathologic cells that are usually to be found in otherwise normal tissue. When followed up by a caustic, such as the acid nitrate of mercury, it may be valuable in various superficial conditions, such as basal celled cancer. The use of the knife is unquestionably the cleanest way of disposing of many lesions, particularly of the non-malignant neoplasms; in the hands of a really competent surgeon the resulting scar is often almost infinitesimal. However, the operation must be surgically clean, the wound must be closed with stitches, and dressings are always required, as well as more or less after-care. A fairly wide margin must always be available. The knife gives the best tissue for pathologic examination.

For heavy work, the actual cautery is probably superior to most of the electric cauteries, for the blade will not burn out so readily, when removed from the tissues; but for light work the electric cautery has several great advantages: it is mechanically easier to operate, and it is easier to keep at a steady heat, either dull red or bright red. An operation can be done with great rapidity, and with the use of a local anesthetic is painless. After operation the wound is perfectly dry and there is no occasion for hemostasis; no dressings are required, for the scab makes its own dressing. Where it is impossible to give much margin, the cautery is the ideal instrument. In cases of malignancy the blood-vessels and lymphatics are sealed and all the neighboring cells are thoroughly cooked; all surgeons are agreed that in malignancy there are fewer recurrences after the use of the cautery than after the use of the knife. And, finally, the cosmetic results are excellent, for the resulting scar is comparatively small and is white, soft and flexible. Tissues are available for microscopic examination, although the edges are completely spoiled.

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Several types of electric cautery are on the market. Hazen has found it convenient to have two; the heavy one is a 110-volt, 2-ampere machine, and the other is much smaller and lighter, but nevertheless very efficient for all small growths.

Hazen believes that the cautery should displace the use of caustics in practically all conditions, and frequently the knife as well.

Caution in Radiotherapy. Among the first to make a therapeutic use of the Roentgen ray in France was Brocq. Having seen many cases of *x*-ray burns followed by chronic dermatitis and epithelioma, resulting from improper use of the rays, Brocq[6] reviews the indications for radiotherapy and warns against over-exposure and improper selection of cases for treatment.

There is danger in too much reliance on filters and radiometers. Most of the burns are the result of the work of inexperienced operators, but he has seen many cases which had been treated by skilled operators.

In Brocq's opinion, radiotherapy is one of the most important therapeutic agents in dermatology and great care should be exercised to prevent it from falling into disrepute. At the present time there is nothing to take its place. But it is very important that it should be used only when every precaution has been taken to prevent accidents.

Radiotherapy in Skin Diseases. The article by Brocq called forth another by Dubreuilh,[7] who adds his testimony to that of Brocq's concerning the abuse of *x*-rays by inexperienced, and over-enthusiastic operators.

It is not alone sufficient to know roentgenology, but it is also necessary to be a clinician and a dermatologist. The *x*-ray is a powerful agent, at best but little understood, very difficult to measure, and fruitful of late sequelae. These dangers are negligible in deep skin cancers when the life of the patient is at stake, but not so when one has replaced a mild vesicular eczema or superfluous hair by a telangiectatic, atrophic scar.

Each year there appears a new announcement that

(6) Ann. derm. et syph., 1917, p. 333.
(7) Ibid., p. 389.

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at last a technique has been perfected for treating hypertrichosis with *x*-ray but each time it is found that the technique is followed by the usual unfortunate results. At present nothing as yet has been discovered to replace electrolysis for hypertrichosis and *x*-rays should never be used.

Epithelioma is the triumph of radiotherapy. Not only can epithelioma be cured when operable but in many cases it will yield when inoperable. The exceptions are most likely to be found in cancers of the lower lip and of the buccal mucous membrane.

GENITO-URINARY DISEASES.

Chronic Induration of the Penis. Hertzler[1] gives a good description of this affection which is characterized by a slowly progressive formation of fibrous tissue in the dorsum of this organ, together with a report of six cases. The lesion begins usually near the root and advances toward the glans, but may begin near the glans and extend proximally. It usually spreads out flatwise over the dorsum but may extend deeply into the septum. It is painless and non-inflammatory, and after reaching a certain size it does not progress. It may cause some burning but its chief significance lies in the fact that it causes impotence because of the exaggerated curve of the penis during erection, due to the mechanical interference of the scar tissue (see Plate VII).

Though this disease has been known in France since La Peyronie first described it, in other countries it was not recognized until a much later date. Ricord nearly a century later redescribed the disease and attempted to define its etiology. He suggested three causes: Inflammation, syphilis and trauma, and two years later made a separate classification for those cases which could not be placed in any one of these categories. This class, it may be said, is, according to the present viewpoint, the only one which, strictly speaking, represents this disease. Those due to either inflammation, trauma,

(1) Jour. Missouri State Med. Ass'n., January, 1917.

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or venereal disease should not be included in the group under discussion.

Of the etiology of this restricted group but little is definitely known. The prevailing theory is that it bears some relation to rheumatism and gout. Kirley was the first to suggest such a relationship. He noted this affection in a gouty patient who had nodules in the palmar fascia and tendon sheaths. Diabetes is present in a large number of cases. Stein recently called attention to the association of this disease with Dupuytren's contraction. The association of Dupuytren's contraction with gout had previously been noted by Paget and Hedges and occurred in one of the author's cases.

The clinical manifestations of plastic induration of the penis are exceedingly characteristic. It begins usually in men past 40 years of age. Usually a burning or a recurvation during erection first causes the patient to present himself for examination. Examination shows an induration, usually near the symphysis. Sometimes several nodules begin simultaneously which afterward become confluent. Rarely does the first manifestation begin near the glans. The induration continues until it gains a length of several centimeters or more, and a breadth of half as much. Sometimes, however, the extension is deeper. A cross-section of the indurated area in such cases presents a T form. Those which were said to have caused occlusion of the urethra did not belong to this disease but were due to some inflammatory trouble.

The tumor is attached to the capsule of the corpus cavernosum but the skin always remains free from it. The corpora cavernosa are usually not directly invaded but in one of the author's cases these bodies contained processes of the lesion.

On inspection, nothing can be discerned when the organ is flaccid. During erection there is a sharp upward curve so that the glans approaches or strongly imbeds itself in the abdominal wall. In some instances, the deviation is said to have been lateral as well as upward. On palpation the induration is readily perceived. The feel is a dense elastic one, exactly like that of a keloid.

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Subjectively, the disturbances are not great. Some spontaneous smarting or burning has been complained of. This is heightened during erection, sometimes to actual pain.

The chief disturbance caused by the disease is that of impotency due to purely mechanical factors, less often to the actual pain present.

In a few cases cartilage, calcareous infiltration or actual bone formation has been noted. In most of the instances noted, the induration was composed of dense fibrous bundles with sparse, spindle-form nuclei. In their structure they closely resemble Dupuytren's contraction, the clinical relation of which has already been mentioned. In structure, this tissue resembles keloids as closely as it does in its physical characters.

The duration of onset varies between four months and one and a half years. In one of the author's cases it was well-marked after three months. Considering the histologic structure the progress is relatively rapid, here again bearing resemblance to keloids.

The disease is so characteristic that but little difficulty should be experienced in recognizing it. The slow onset, the peculiar feel, and the potential limitation it causes in the function of the organ establish the diagnosis.

But two plans of treatment deserve consideration: Roentgen ray and operation. Judging from the excellent results obtained by the ray in keloids and the histologic resemblance of the disease to the keloids, benefit from the ray was to be hoped for. These hopes have not been realized.

In the author's two patients who were operated on, anatomic cure with functional improvement resulted, though one can hardly speak of a cure in either case. The patient who received one treatment by the Roentgen ray was not improved. This is not to be wondered at, since Bernasconi's case required eighteen treatments in order to complete a cure. From the foregoing, it is evident that any line of treatment is unsatisfactory.

Plastic Meatotomy. The operation of meatotomy, says J. L. Hamilton,[2] is performed for the relief of a

(2) Glasgow Med. Jour., September, 1917.

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condition which occurs frequently in young male children, namely retention of urine from ulceration round the urinary meatus. This ulceration is found after circumcision, and is due to the fact the phimosis produces, in many cases, a slight pouting or prolapse of the mucous membrane of the urethra. When the child is circumcised, this protruding mucous membrane is exposed to friction from napkins or clothing and becomes eroded, forming a ring of ulceration round the meatus. The passing of urine over the raw surface being painful, the child retains the urine as long as possible. Meanwhile, a crust forms on the ulcerated surface, sealing the urethral orifice, and so forming an obstruction. When the bladder is full—or overfull—this crust must be forced off from the meatus before urine can be passed, only to form again in the interval before urine is again passed.

The condition need not be confused with other forms of retention, since it is easily recognized on examination. The mother's story is that the child is cross, crying more or less constantly. He passes urine less often

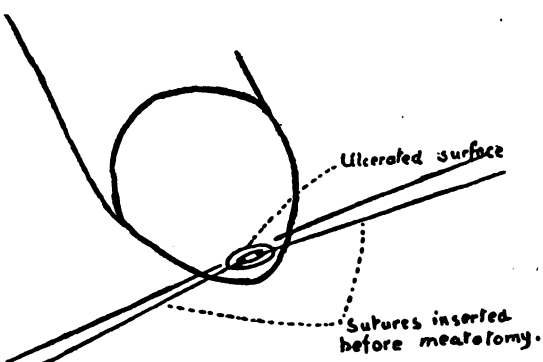

Fig. 2.

than normally, and screams when he does pass it. In older children the complaint may be of nocturnal incontinence, and in these children the bladder will be found to be distended, the incontinence being due to overflow. This state of affairs gives rise to much discomfort, which may continue indefinitely, since the situation of the ul-

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cer exposes it to constant irritation and makes healing almost impossible. In the treatment of this form of retention, the operation to be described—devised by Mr. Alex. MacLennan—has proved very successful.

An intestinal needle is used, so that the suture may plug the track of the needle through the glans and thus

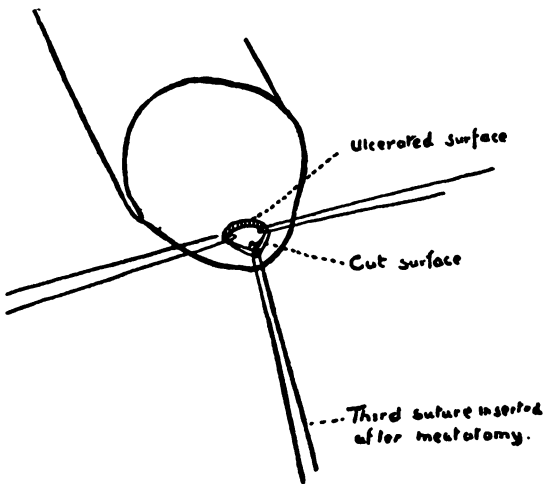

Fig. 3.

prevent hemorrhage. The needle, threaded with catgut, is passed into the urethra and brought out through the glans at one side beyond the ulcerated surface. A similar suture is inserted on the opposite side of the meatus, and by these two sutures, as shown in Figure 2, the sides of the meatus are pulled apart, while the glans is divided down, by scissors or scalpel, from the lower margin of the meatus for a distance of an eighth to a third of an inch, varying with the size of the ulcer and the tightness of the meatus.

The third suture is shown in Figure 3. It also is inserted from inside the urethra through the glans, and is placed at the end of the incision, *i. e.*, at what is now the lower angle of the meatus. The three sutures are tied with the knots inside the urethra to keep the edges of the meatus apart.

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This operation has been found to be invariably successful. The retention disappears immediately, and the ulcer is quite healed in a few days.

Predominance of the Left-Sided Bubo. In a series of fifty cases of chancroid and bubo reported by Montpellier,[3] the distribution was as follows: Left, twenty-nine; right, thirteen; bilateral, eight; total, fifty.

Even when the chancroid was found on the right side of the penis the bubo was frequently located in the left inguinal region. The author is of the opinion that there must be a confluence of the penile lymphatics on that side.

Tumors of the Bladder. From a study of 113 tumors of the bladder that have come under the observation of Leo Buerger[4] at the pathologic laboratory of Mount Sinai Hospital during the past ten years, and from a study of other vesical tumors, more than twenty-five in number, where the material, however, was not sufficient to be included in the series, he has come to the conclusion that the pathologic diagnosis of carcinoma is possible in most cases[5] (*vide* Geraghty).

Among these 113 tumors there were fifty-five papillomata, forty-five papillary carcinomata, and five squamous carcinomata.

Certain morphologic criteria were accepted as indicating the existence or the acquisition of malignant traits in any given tumor. These criteria were found to be present in parts of the tumor that were accessible, so far as they could be reached by cystoscopic instruments, and so far as adequate portions could be removed for histologic examination. The changes indicative of malignancy occur, not, as heretofore assumed, in the "depth" where they may escape our diagnostic methods, but occur first in the epithelium, not far from the surface, either with or without areas of infiltration.

A test of the morphologic criteria proved conclusively that they were trustworthy and that, if adopted, they lead to correct diagnosis. Many of the other loosely accepted notions regarding the malignancy of papilloma

(3) Ann. des maladies, vén., 1917, p. 434.
(4) New York Med. Journal, Oct. 28, 1916.
(5) See article by Geraghty, pages 114-116, this volume.

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per se were found to be fallacious. Only in one tumor out of 113 was a papilloma found to infiltrate and still retain "normal" cellular characteristics.

In short, a trustworthy pathologic diagnosis and the possibility of differentiating between carcinoma and papilloma depend upon our opportunities of obtaining material and upon our ability to recognize the criteria laid down as indicative of malignancy; that the latter are present the author's series of tumors has definitely shown.

Treatment of Bladder Tumors. The selection of the proper treatment for tumors of the bladder depends upon the determination of many factors, most important of which is the ascertaining of the nature of the tumor. Other factors, says Geraghty,[6] such as position, extent, and number of tumors, presence of metastases and complications, will all play rôles in determining the best method of attack.

For a number of years the author has systematically excised pieces of bladder tumors and studied them with care histologically, in an endeavor to see if there was not some histologic picture which would clearly indicate the selection of the most suitable form of treatment. In the vast majority of cases, however, he is not able from the histologic picture alone to decide with accuracy whether the tumor will respond to fulguration or whether more radical procedures should be adopted. Repeatedly, in his experience, excised pieces of papillary carcinoma are found to have a histologic picture no different from that seen in the average malignant papilloma, while the clinical examination indicated most extensive infiltration, which was subsequently corroborated by the course of the disease. As a means of differentiation between malignant papilloma and papillary carcinoma, cystoscopy, combined with other clinical methods, is a greater aid than the histologic picture alone. Finding, on cystoscopic examination, the presence of necrotic papillae on an otherwise benign looking papilloma, the presence of edema around the margin of the tumor or nodules in the mucous membrane in the neighborhood of the tumor,

(6) New York Med. Jour., Oct. 28, 1916.

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the presence of an intractable cystitis, and, when tumors are situated on the posterior bladder wall, feeling on rectal examination the slightest induration therein, are points in the differential diagnosis which have served best. It must be admitted that none of these conditions may be present and the tumor may still have invaded the bladder wall. When in doubt concerning the nature of the tumor, Geraghty's practice has been to adopt fulguration as a therapeutic test. After a few applications of the fulguration current, it can usually be determined whether the tumor be suitable for this form of treatment. When the surface of the tumor is vigorously fulgurated and the slough does not separate, or when it becomes covered with calcareous deposit, this is evidence of advanced malignant changes in the deeper portions of the tumor.

The experience in the Johns Hopkins clinic in recent years indicates that benign and malignant papillomata should be treated by fulguration; excision or resection should not be practiced except where intravesical treatment is impossible or very difficult. Radium has been a great aid in the treatment, particularly of the malignant papillomata, and the best results have been obtained when the radium was placed directly against the tumor. When the tumor is a papillary carcinoma, resection should be practiced by a technique which will reduce to a minimum the dangers of implantation or recurrence. Radium as yet has not given results in this type of tumor sufficiently encouraging to warrant the employment of it in preference to resection in cases which are considered operable. Following resection, cystoscopy should be performed at an early date, and at frequent intervals, especially for the first year, and if recurrence be noted, it can occasionally be successfully treated by a combination of fulguration and radium. Unfortunately, a large percentage of cases are first seen with the disease so extensive that nothing more than palliative measures can be adopted.

Cystoscopic Rectovesical Transillumination. Digital examination of subvesical structures by rectum is at best uncertain. The examining finger is a short instrument and a pathologic condition must be placed low

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down to be thus discovered; also, it must be distinctly palpable as to contour and consistence to give information of any certainty. To decide beyond a doubt that we are dealing with disease, is at times impossible, and anything that aids in diagnosis in this region of more or less uncertainty has a distinct value. For this reason Pelouze[7] has made the application of the old method of transillumination, to these structures.

Fig. 4. Rectal lamp and carrier.

If one insert the cystoscope into the bladder, dilate the viscus with water, introduce an electric bulb into the rectum, and turn out the cystoscopic light, it is possible to transilluminate the intervening structures. So thoroughly can this be done that the tiny blood-vessels of the base of the bladder are distinctly seen, and changes in tissue thickness and density can be accurately determined, and the ureter followed for a little distance.

For this purpose, the author had made a curved shaft for carrying a large transillumination lamp. This curve was found necessary because the straight shaft not only restricted lateral motion but pushed too sharply into the base of the bladder (Fig. 4). The lamp gives a very brilliant light, and, being surrounded by an air chamber, there is no danger of producing a burn.

The technique is extremely simple, offering no difficulty whatever to one moderately skilled in the use of the cystoscope. With a little practice, it is hardly necessary to light the cystoscopic lamp for purposes of orientation, but this can easily be done from time to time more accurately to locate a given area.

Surgical Treatment of Acute Epididymitis. From the results observed in a series of eleven cases, Mc-

(7) New York Med. Jour., Oct. 14, 1916.

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Kenna[8] concludes that surgical interference is necessary only when the patient is suffering excruciating pain. When this procedure is carried out, it is quite necessary to divide the fasciae so as to free the tension from the testicle as well as from the epididymis. Patients are less apt to be impotent if the posterior wall be divided carefully and the pus drained off than if the pus be left for Nature to absorb. "A blind-stab operation is that of a faker and should not be considered." It is enough to expose the epididymis and drain it; all the fasciae should be free.

It is not necessary to split the epididymis but only the infected chamber which stands out clearly.

Seminal Vesicles in Persistent Non-gonorrheal Infections. It is well known that the seminal vesicles may become involved during the course of a gonorrheal urethritis, and, if the process remain active in the vesicles, may prolong urethral infection in a most stubborn manner. The constant or intermittent feeding of new infection into the prostatic urethra keeps active the inflammatory processes of the urethral mucosa, just as inflammatory processes in the vesical mucosa are activated by renal infections.

It is probably not so universally recognized, according to J. T. Geraghty,[9] that the seminal vesicles, when the seat of a non-gonorrheal or pyogenic infection, may result in prolonged suppuration of the posterior urethra and trigon. These infections may be even more stubborn than those of gonorrheal nature. It is surprising how many of these long-standing bacillary and coccus infections involving the posterior urethra and at times the bladder have been secondary to unsuspected vesiculitis.

In some cases, the infection assumes the form of a bacteruria with occasional exacerbations in which a visible amount of pus can be detected and with periods of more or less urinary irritability. Sometimes the patient is seen with a frank cystitis and with a history of repeated previous attacks. Under treatment applied to the local condition, and even often without definite

(8) Surg., Gynec. and Obstet., December, 1916.
(9) Jour. Amer. Med. Ass'n., March 10, 1917.

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treatment, the symptoms subside and the urinary condition may improve until the most careful examination is necessary to demonstrate the presence of bacteria in the urine. After a varying length of time the process repeats itself. Most often the urine at all times supplies definite evidence of infection and may be continuously cloudy. During the intervals in which the infection is at a low ebb or quiescent, examination of the urinary tract may disclose very little abnormal, and frequently nothing which could explain the persistence of an infection. When exacerbations occur, definite lesions are found; but with the disappearance of the lesions, the infection does not disappear from the urine.

The fixing of the responsibility on the seminal vesicles as the source of the continued or recurrent infection is not always easy. In cases in which epididymitis occurs, and especially when there is recurrent epididymitis, the diagnosis of an active infection in the vesicles becomes reasonably certain. In many cases the presence of a vesiculitis may be readily determined by palpation; but it is surprising in what a large percentage active foci are present in one or the other vesicle and still careful palpation may reveal very few changes. The diagnosis of vesiculitis in many cases depends entirely on changes which can be detected by palpation, and consequently it is very inaccurate. When infection is already present in the posterior urethra, the finding of infection in the expressed seminal vesicle secretion is utterly valueless because it is impossible in such cases to obtain the seminal vesicle secretion uncontaminated. Neither are we always justified in considering that active infection may be present in the seminal vesicles simply because of changes which are detected by palpation. An old inflammatory process may have been present long before, and the induration is the result of this process, which has entirely subsided.

In some cases, the determination of the presence of infection in the vesicles must be arrived at by a process of elimination. The occurrence of a persistent bacteriuria requires some focus continually feeding infection into some point of the urinary tract where there

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is no obstruction to urination and no residual urine is present. It is well known from repeated experiments that if organisms be injected into a normal bladder, in a comparatively short time they will entirely disappear from the urine. We know again that if the kidney be infected and that secondarily to this there be present a simple cystitis, the removal of the renal infection will be shortly followed by disappearance of the vesicle infection.

Six cases of the type described above have been under observation by Geraghty for periods varying from a few months to many years. The kidney as a source of infection was eliminated in each case. The patients had been treated at varying times by prostatic massage, instillations, irrigations and stripping of the seminal vesicles, but in none of the cases was it possible to eradicate entirely the infection, and the patients presented themselves at different periods with exacerbations. In two cases the infection took the form of a persistent bacteruria, one case being due to a colon bacillus and the other to staphylococcus. Of the remaining four cases, one was a staphylococcus infection and the other three were due to colon bacilli. In the latter four cases pus and organisms could always be found in the urine, the amounts varying at different periods.

In the belief that the seminal vesicles were probably responsible for these stubborn and resistant infections, it was determined to do a vesiculotomy in each case. In two cases a recurrent epididymitis pointed strongly toward the seminal vesicles as the most probable cause. In three cases there were definite changes in the seminal vesicles which could be detected on palpation. In three of the cases no changes could be detected, and they were apparently normal on palpation. The results of the vesiculotomy in each case were immediate and most gratifying.

Spirochetes in the Urine. A widespread interest in the increasingly numerous group of diseases known to be caused by spirochetes, and the consequent desire for a rapid and sure means of diagnosis, have brought

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forward the possibility of recognizing such cases by finding the spirochetes in the urine.

An interesting report is made by Lieut. Stoddard,[1] M. R. C., U. S. Army, of the examination of 100 men at U. S. Army Base Hospital No. 5.

That spirochetes may actually be excreted by the kidney in diseases of spirochetal origin is a fact resting on the reliable experimental evidence of the workers on spirochetosis icterohemorrhagica. Their animal experiments have demonstrated that spirochetes occur in the urine which have the same pathogenic effect on guinea-pigs as the organisms found in the blood. Obviously, a similar excretion may occur in other diseases, and thus afford an easy means of diagnosis.

Certain observations made recently at this hospital, however, show a source of error in a procedure of this kind. It was found, in brief, that:

1. Spirochetes are not uncommon organisms in the urethra of men without history or symptoms or relapsing fever.

2. Many different varieties are found.

3. Some of the varieties seen are morphologically closely similar to pathogenic varieties.

4. The spirochetes occur so definitely within the urethra that they are an obvious source of contamination in uncatheterized specimens of urine.

5. They are a sufficiently dangerous source of error, even in catheterized specimens, to deserve attention in careful work.

6. It is possible that a staining reaction or some other morphologic character may be discovered to differentiate microscopically the common and harmless from the pathogenic spirochetes. Since the pathogenic spirochetes are still in the process of discovery, such methods are not universally applicable.

The work was initiated by the finding of spirochetes in centrifugalized specimens of the urine of a nephritis patient with relapsing fever. The urine was divided into two portions, and the sediment of the first portion passed found to contain from ten to twenty times as many spirochetes as the later portion passed. The ob-

(1) Brit. Med. Jour., Sept. 29, 1917.

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vious intra-urethral or peri-urethral source was investigated by films made with a platinum loop, and spirochetes of the same variety found in great numbers. It seemed probable that such spirochetes were a common saprophytic organism rather than a localized evidence of a general spirochetosis. Consequently, other patients with and without relapsing fever were investigated similarly. Spirochetes were found in the urine and in urethral smears from five out of fourteen men. In only one case were spirochetes found locally, but not in the urine. That the spirochetes do not have their ultimate origin in the urine seemed probable because by passing the urine in successive portions a part toward the last could be obtained in which no spirochetes could be found. Such methods can not be depended upon, however, to eliminate the intra-urethral parasites.

When it was evident that spirochetes of intra-urethral origin could frequently be found in the urine, a study was made of 100 men without history or symptoms of any fever of a relapsing type. Fifty of these were hospital patients with miscellaneous medical and surgical conditions; many of them were gassed cases. They were selected entirely haphazard. The other fifty consisted of U. S. A. men who came to France from America in early June or the latter part of July.

In each case, films were made with a platinum loop from the distal one-third inch of the urethra and from the region about the urethral orifice. In making the urethral smears as a rule the meatus was parted and the loop introduced with as little contact with the orifice as possible. In several cases the anatomic conditions were such that contamination from extra-urethral sources undoubtedly occurred, and in other cases faults in technique may have been present. Consequently, no rigid separation of sources is possible. The occurrence in several cases of spirochetes in the urethral but not in the other smears is evidence of their intra-urethral origin, in these particular instances at least.

The spirochetes similar in type to those found in the urine of patients with "trench fever" or to Noguchi's description of *Spirochaeta icterohaemorrhagiae* are grouped with other spirochetes obviously not similar

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to *S. refringens.* Figures are then given for all spirochetes, including *S. refringens.* The latter figure is not as significant, for the *refringens* type is so different from the others as to cause little confusion.

In the first series, consisting of fifty hospital patients, spirochetes (excluding the *S. refringens* type) were found in 46 per cent. of the urethral films. If *S. refringens* be included, the total incidence of all kinds of spirochetes amounts to 56 per cent.

In the second series, of fifty well U. S. A. men, intraurethral spirochetes (excluding *S. refringens*) occurred in 20 per cent. of the cases. The total incidence of all spirochetes, including *S. refringens,* was 22 per cent.

It is believed that the smaller percentage in the U. S. A. men is due to the better health and hygiene of the subjects. It is very probable that saprophytic organisms increase on these as on other mucous surfaces in conditions of low vigor (or hygiene). That this be the explanation here is suggested by the correspondingly smaller percentage of occurrence of the *S. refringens* types.

Since these differences are probably not of great significance, it is of interest to average the figures of the two series to get the incidence in the whole series of 100 men. When this is done it is found that spirochetes of all types but *S. refringens* occur in 33 per cent. of the cases. Including *S. refringens,* spirochetes are found in 44 per cent. If the figures for the spirochetes present near but not in the urethra be added, the percentage of spirochetes in either one or the other situation becomes 38 per cent. If *S. refringens* be included, the incidence is 46 per cent.

Morphologic studies were made principally with the tannic-acid-carbol-fuchsin method, but the Fontana, the India-ink, Giemsa, and the Leishman and Wright modifications of the Romanowsky methods were tested. As a rule, the stain with carbol-fuchsin was definite, but some slender spirochetes were found which stained with difficulty. The Fontana stain was usually definite and clear. Loeffler's methylene-blue stained not at all, or very faintly. Carbol-fuchsin, without previous mordant, heated as for tubercle bacillus (but not decolor-

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ized), stained moderately well, but less satisfactorily than the mordanted stain. Flagella were not made out, although there was frequently extremely fine tapering of the extremities.

No noticeable difference could be made out between the spirochetes found in the urine of patients with trench fever and those found in the urethral smears of other individuals.

The smears from the peri-urethral region were more likely to contain a greater proportion of spirochetes of the *refringens* type, while slender, closely-coiled spirochetes were perhaps more likely to be predominant in the urethral smears.

In one film many different varieties are often present, including frequently organisms similar to the description of *Spirocheta icterohaemorrhagiae.*

[The presence of spirochetes in the urethra and about the meatus of normal men obviously offers many opportunities for mistakes in the search for *Spirocheta pallida* by inexperienced workers.—EDITORS.]

VENEREAL DISEASES.

PROPHYLAXIS AND SOCIOLOGIC ASPECTS.

Venereal Disease and Its Prevention. The commonest source of venereal infection now is demonstrably not the professional prostitute. Molesworth[2] says that the proportion of cases infected from amateur sources to those from professional prostitutes during the past five years is about 2 to 1; and that the total number of cases has greatly increased during the same period.

Several factors complicate the problem, especially the influence of the war; but this paper deals principally with the civil male cases. There is the moral pessimist's explanation that the morality of the times has deteriorated to an extent sufficient to account for the change; there is the fact that the women are entering more and more into industrialism, and that the less successful may be forced to supplement their wages by

(2) Med. Jour. Australia, September, 1916.

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clandestine prostitution, or become willing to obtain luxuries from men whose mistresses they become; there is the question of the influence of alcoholism on the incidence of these diseases and there is the influence of public ignorance of the risks and importance of these diseases to be taken into consideration.

1. *The War:* As these figures are almost exclusively of male civilians infected, the enthusiasm of ardent young women for soldiers would rather diminish the popularity and opportunity of the civilian. It is a fair assumption to regard the very numerous cases occurring among the soldiers as the direct effect of the war fever on the male portion of the community. The secondary effect is that produced by the infection of a large number of women by soldiers and the development of a sexual appetite in a large number of girls in whom it would probably have lain dormant under peace conditions until marriage, or at any rate for some years longer. These women in turn may become willing to obtain gratification of their stimulated sexual appetite from civilians, and incidentally infect them; but this influence must be discounted on consideration of the fact that no military or female figures enter into the discussion.

2. *The Influence of a Supposed Moral Deterioration:* For several reasons the author does not believe it to be true in the sense implied by the moral pessimist.

First, a change in moral tone has always been of slow and almost imperceptible progress, when a whole community or people is considered, while the increase of venereal disease is recent and rapid.

Second, a real deterioration of moral tone would not be limited to the sexual side; but a decline in morality would certainly be accompanied by other signs, such as an increase of drunkenness and crime. So far from this being the case, the reverse is true.

3. *The Emancipation of Women, and Their Entrance into the Industrial Arena:* The influence of this factor is real and active, since it is fairly closely contemporaneous with the increase of venereal disease, and obviously by bringing young women into more constant and less supervised association with men of all sorts it will

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afford more opportunity and less restraint in sexual matters. At the same time, it is inevitable that a considerable proportion of these women will absorb the moral tone of the man of the world, and regard sexual satisfaction as a right, or at least as a venal offense rather than as the unpardonable crime. This emancipation, moral and otherwise, will necessarily result in the diminution of resistance to the sexual impulse even in the better types and more educated individuals. This is in many ways a great pity, though the innocence arising from lack of temptation or opportunity is but a poor imitation of real virtue. There are two classes which will exert a considerable influence upon the problem. There is, first, the class which, not earning enough to make both ends meet, is forced to adopt prostitution as a second string. However, a large proportion of this class will, by the nature of their object in adopting this course, and their needs, demand and accept payment in cash, and must be regarded as professional prostitutes, although strictly speaking, they should be regarded as amateurs, because, though plying the trade, they are largely ignorant of its risks, and the necessary precaution, and being less dependent upon its profits, they are less careful of their professional reputation for safety and cleanliness.

The next class is that composed of women who, though earning enough to provide the necessities of life, still find themselves unable to afford what might be regarded as luxuries; but with which they are familiar by reason of their daily occupation in town. A woman of this class soon learns that all these things can be obtained, if she in turn be willing to provide other entertainment to the donor. Soon becoming initiated if she have little or no restraining influences to a perfectly normal sexual desire, she rapidly becomes less difficult to persuade, and soon becomes willing to accept any offer that promises the double pleasure of sexual gratification and, say, a motor drive. Either not recognizing the disease or its danger, or being unable to obtain proper treatment without betraying her state to friends or family, she neglects it or forgets it, but infects all her lovers. This is the class which, according to Molesworth's investi-

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gations, is the source of infection in 60 per cent. of the men attending the venereal clinic at the Royal Prince Alfred Hospital.

4. *The Influence of Alcoholism:* It has not even been suggested that there has been an increase of drinking among women, while it is a well-known fact that, of late, there has been a marked diminution in the consumption of alcohol *per capita,* whereas the venereal cases increase in number.

5. *The Influence of the Public Ignorance of the Risks of Infection with These Diseases, and the Seriousness of Them:* This is a very important factor, especially when taken in conjunction with the entry of young women into industrialism. The times have changed; young women are to a large extent emancipated, and, therefore, more exposed to temptation, and yet their training in sexual matters remains the same early Victorian negative quantity, the same thing holding, though to a less extent, in the case of boys. Public ignorance acts in another way also, in that the vast majority of the lay public believes that sexual intercourse with a prostitute is very likely followed by venereal diseases, while the so-called "square girl" is safe.

The professional prostitute is responsible for fewer infections than the young women of easy virtue who lend themselves for love to an evening excursion in a car or boat.

[Men rarely give us a history of infection by a professional prostitute. Street walkers, cabaret habitués and adulterous wives seem to be the most common sources of infection.—EDITORS.]

A very powerful influence upon the incidence and rapid increase in venereal disease is the recent legislative tampering with the action of a moral safety-valve. Prostitution is the oldest profession in the world, existed before our civilization was dreamed of, and will survive long after it is forgotten. That it carries in its train many evils is universally admitted; that it meets a constant public demand is proved by its long and flourishing life. The question is whether the laws at present operative in New South Wales will produce the results intended. The laws passed recently

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were principally directed towards (1) breaking up of public brothels; (2) prevention of solicitation on the streets, and (3) detention in prison of prisoners found to be suffering from venereal disease until cured or rendered non-infective. The only one of these which could have been at the same time possible of achievement and productive of good was the last, and that was crippled by the fact that, by a legal flaw, only those sentenced to imprisonment could be so detained, while those punished by fine had to be set free.

Of the other two—the prevention of solicitation in the streets—obviously impossible of attainment, has since been shown to be a farce, and the police, with the best efforts, fail to do anything really effective.

The most disastrous part of the legislation is the denial of a home to the professional prostitute. Under the Wade law, not only are congregations of prostitutes in public brothels broken up, but the landlord of any building, who, on notification by the police that one of his tenants is a prostitute, and is using her room for the purpose of prostitution, fails to evict her, renders himself liable to a severe penalty, and the tenant is evicted by order of the magistrate.

The breaking up of brothels can only result in the disorganization, not the elimination, of prostitutes, since few are fitted and still fewer inclined to take up other occupations. Hence you have only succeeded in multiplying the brothels while reducing their size.

Moreover, as the prostitute is prevented, on pain of eviction, from practicing her profession in her own room, one would expect that she would either make use of a room hired for the night, or follow the amateur into the open air. In either case, apparatus and facilities for cleanliness are inadequate or altogether absent. Again, the woman is made poorer and more desperate by persecution. It is dangerous to remove from her the necessity of maintaining for the house a reputation for cleanliness and freedom from risk of infection, since she has now an ever-changing clientele and domicile. Moreover, as it is hardly conceivable that a professional prostitute should escape infection, and as it is only by prosperity that she is enabled to seek adequate treat-

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ment and to become temporarily non-infective by the exercise of cleanliness, so that the practice of her profession may be rendered reasonably safe, it is only to be expected that prostitutes should become a source of greater danger than before, while only slightly if at all less numerous.

Men, accustomed to regular sexual intercourse, are the least likely of the community, which, as a whole, can not be expected to exercise continence, to live without sexual gratification, and deprived of their usual means of obtaining this, will search for new ones. Added to this, there is the inevitable impression conveyed to the mind of the public that the persecution of the unfortunates must, at least in part, be due to their being in the highest degree dangerous, in consequence of which the votary, thanking the gods that he has so far escaped, lightly embraces a new faith, and proceeds to worship at a new shrine—that of the amateur.

Under these circumstances, is it reasonable to expect the amateurs to be as safe as the professional who knows the risks, the means of avoiding them, and whose livelihood depends on her reputation for innocuousness?

Solicitation has not been banished from our streets. The solicitation, it is true, is furtive; but there it is, all the same.

Persecution of the brothel-dwellers has not resulted in the diminution of facilities for sexual intercourse. An inspector of police in Sydney says that the number of assignation houses, especially in connection with restaurants of the poorer class, and conducted chiefly by Greeks and Italians, are legion. A room for the night and no questions asked; if quitted in an hour so much the better. The facilities are few and cleanliness difficult. The patronage they enjoy, however, is constant and large, and they are used freely by both the professional prostitute and the amorous amateur.

The author believes that the problem can be best solved by first:

1. Legislation:
   (*a*) Recognition and regulation of prostitutes.
   (*b*) Notification of venereal disease by attending physician.

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2. Education:
   (*a*) Of both men and women in military units, universities and factories.
   (*b*) Adolescent boys and girls should be given careful instruction.
3. Treatment:
   This should be available to all in both day and night clinics, supported by the state, and should consist in intensive arsenobenzol medication.

War and Venereal Diseases. Assistant Surgeon Tullidge, U. S. N.,[3] advises, first, careful supervision and frequent inspection of the men with the establishment of a severe penalty for failure to administer the prophylactic provided; second, providing carefully inspected, and restricted districts or houses of prostitution conducted especially for the men in the service under military supervision. This practice is successfully employed in Italy, Germany, Austria, and until recently in France and England, with surprisingly satisfactory results. With the establishment of these houses during the course of venereal inspection of the men, which was held in the German army every two weeks, the appearance of any venereal disease could be traced directly to the seat of infection and the prostitute placed under arrest and sent to a government hospital, where she remained until pronounced cured. For those living at sea on board ship the establishment of such districts or houses would be advantageous for the men given liberty on shore, and would, with the prophylactic, almost eradicate the disease from the naval service.

The two army prophylactic treatments for syphilis and gonorrhea have received wide attention and consideration. The former army "K" packet, containing a solution of 20 per cent. protargol or 10 per cent. argyrol, a medicine dropper or syringe, and a vial of 30 per cent. calomel ointment, was effective when used not only as a prophylactic, but within two hours after intercourse. In a section of over 1,700 militiamen who received this treatment properly on the border during

(3) Med. Record, Sept. 22, 1917.

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the last mobilization, thirty-eight developed venereal diseases. Ten were primary luetic sores, ten chancroids, and the remaining eighteen gonorrhea, which was complicated in seven cases with one of the former infections. With these results, this treatment could hardly be called successful and the large percentage of infections resulted either because of the failure of the men to apply for the treatment within the prescribed time after intercourse or because of the failure of the ointment to come up to its declared standard of efficiency.

With these possibilities in view, and with the idea of providing for the men in the naval service who are unable to obtain treatment within the prescribed two-hour period necessary for proper results, Surgeon Robert A. Bauchman, U. S. Navy, after an exhaustive investigation and experimentation, both at home and abroad, prepared an ointment similar to Metchnikoff's preparation. This ointment, which contains 33 per cent. calomel reinforced by 1 per cent. trikresol, he placed in a collapsible tube carefully prepared and enameled throughout inside to prevent a degeneration of the mercurial substance by contact with the metal of the tube itself. A soft rubber tapering nozzle one and one-half inches long, which may be introduced well up into the meatus beyond any possible area of infection, covers its mouth. This preparation he claims is most efficacious, and from the many reports of trials given it and the excellent results obtained in cases in which Tullidge has recommended its use, he is convinced that it has decided advantages over all other prophylactics of its kind at present in use. It is smaller in bulk, more compact, and therefore more easily handled. If carried upon the person at all times and properly used both before and immediately after intercourse, or within an hour, it has decided advantages over all other treatment.

Military Hospitals for Venereal Disease. In an official report Pautrier[4] sets forth the many advantages to be gained by having all venereal diseases in one department which should be located in close proximity

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to centers for the other specialties in order that the syphilitic may have the benefit of the advice of men in other departments, especially those of the eye and ear. These hospitals are now well-organized in France.

The great need for special centers is proved by a citation of many cases of syphilis which have been hospitalized for months because of the failure of the attending physicians to recognize and to treat properly the disease. He recommends that the building should be so constructed as to have an enclosed court, thus allowing out-door exercise without giving the men their freedom, which is frequently followed by infection of the civil population. He urges the necessity of strict interdiction of the use of tobacco and of the addition of a dentist to the staff to care for and to prevent the development of mercurial stomatitis.

In order to insure correct diagnoses and proper treatment, he insists that only well-trained dermatologists and syphilographers be admitted to the staff. He also calls attention to the great danger of having the Wassermann tests done by any other than a highly skilled serologist.

Treatment in primary and secondary cases should consist of six injections of novarsenobenzol at weekly intervals and intravenous injections of cyanate or biniodide of mercury.

As a means of combating the spread of venereal diseases in the civil population and thence to the military he advises the creation of auxilary free clinics, both day and night, for the civil population. In this way a great many cases of venereal disease in the civil population have been found and treated.

Gonorrhea.

Physiologic Therapy in Gonorrhea. In order to treat this disease physiologically not only should the physiology of the patient be taken into consideration but also the physiology of the micrococcus. The gonococcus is grown with difficulty in an artificial culture medium. The normal urethra is continually bathed in an acid chloride solution favorable for germ cultivation. Ac-

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cording to the "physiologic" therapy of Geyser,[5] sodium bicarbonate is administered to render the urine alkaline, then all sodium chloride intake is stopped by ordering a salt-free diet. This results in alkaline sodium chloride free urine which offers a poor medium for cocci proliferation.

The temperature of the urethra during this infection ranges from 99° to 103° F., a temperature favorable for the germ proliferation. By inserting an ordinary steel sound attached to one pole of a diathermic apparatus, the temperature can easily be raised to 108° F., in the urethra. This temperature, if maintained for at least one hour or more daily for three days, kills the specific cause of the infection.

Since iodine is one of the best germicides known and since the introduction of the sound requires lubrication, about fifteen drops of a colloidal iodine preparation are injected into the urethra. All iodine compounds are very unstable, but when the sound and the tissues in contact with the iodine become heated, nascent iodine is liberated. This iodine in a gaseous state will enter tissue during the diathermic process better than any oily or watery iodine or silver solution. After three days of this kind of treatment all active treatment should cease and the patient should be instructed to douche the urethra at least twice daily for three more days with water as hot as can be comfortably borne.

A smear must be taken daily for control purposes. The average case of uncomplicated gonorrhea can be cured in one week, according to Geyser.

Acute Gonorrhea Treated with Vaccines. An interesting study was made by Captain Lumb,[6] R. A. M. C., of the effect of the intensive use of a mixed gonococcus and staphylococcus vaccine combined with frequent irrigations with potassium permanganate in acute gonorrhea.

The method is as follows: The patient stays in bed for the first three days, getting up only to irrigate in the morning and again in the afternoon. Milk diet is

(5) New York Med. Jour., July 7, 1917.
(6) Brit. Med. Jour., Oct. 6, 1917.

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ordered and an unlimited quantity of barley water allowed. Aperients are given regularly as necessary to keep the bowels freely open. Irrigation is commenced with 1 in 8,000 potassium permanganate on Janet's system (*vide* article by Burke, pp. 136-139), the container being placed 5 feet above the patient, who is instructed to wash out thoroughly the anterior urethra first and then to get the solution into the bladder. A dose of 50 million gonococci is given on the first morning, and urotropin, according to the following formula, for five days.

℞	Hexamethylenaminae	66
	Aquae 30	
℞	Acidi sodii phosphatis 1	33
	Potassii citratis	66
	Syr. aurantis 2	
	Inf. buchu .....o. c. 30	

Dose: 30 c.c. of each, mixed at time of taking, t. i. d., p. c.

On the second day irrigation is carried out morning and afternoon as before, and the vaccine is given again on the third morning, the dose being 100 million. By the fourth day the discharge in most acute cases has diminished to a small drop and the patient is allowed to get up and go about as usual, taking a moderate amount of exercise. He now irrigates with 1 in 6,000 potassium permanganate and the diet becomes an ordinary one, except that fish or a *small quantity* of meat is allowed, alcohol and condiments being forbidden. On the morning after getting up, a four-glass urine test is made and used as the guide in further treatment. On the fifth day, the medicine is stopped and another dose (60 million) of gonococci given, irrigation being continued as before. The patient then passes a two-glass urine test, on alternate days, and the treatment is modified as considered necessary. On the ninth day he receives a dose of 100 million gonococci, and a bougie is passed on the tenth day, the urethra being massaged if the glands be involved. The bougie at this stage is valuable in three ways:

1. It allows the massage of Littre's glands.

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2. It reveals any tendency to stricture.
3. It has a stimulating effect on the mucous membrane.

On the thirteenth day, a third dose of 100 million is given, and by the sixteenth day, when it is again repeated, the discharge has almost invariably ceased. The urine in both glasses is clear, though the first one may still contain a few flakes. The patient at this stage is taking as much exercise as possible, playing games every afternoon and eating a full diet. If under these conditions no discharge be apparent, the irrigation is changed to 1/1,000 zinc sulphate or 1/4,000 zinc permanganate for two or three days, and then all treatment stopped. The urine is examined as before and a final dose of 50 million gonococci given two or three days after all treatment has ceased. If the patient be not free from active gonorrhea, this "provocative" dose invariably gives rise to signs in the urine, or an obvious discharge, within twenty-four hours, and this is therefore a most valuable test. If the urine remain clear after this, the case is watched for another three days and then considered clear.

The general effects on the patient can be classified as follows:

1. Mental relief at the rapid disappearance of the discharge.
2. Rapid disappearance of pain on micturition.
3. Rapid disappearance of pain on irrigation.
4. Exercise can be taken without delaying the cure.

The mental state of the gonorrhea patient is very important, and anything which tends to turn his thoughts away from the site of the disease and associated ideas is valuable. The actual injections tend to do this, but far more valuable is the rapid diminution in discharge, which convinces the patient that he really is getting over the attack.

Pain on micturition and during irrigation speedily disappears, considerably increasing the patient's comfort, whilst he can lead an ordinary life and take plenty of exercise without delaying his recovery. No relapses have to be recorded so far, though nearly every case has returned direct to duty at the front.

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The results of 500 consecutive cases show that 222, or roughly 44 per cent. of the cases, were complicated. This is accounted for by two factors: (1) active service; (2) lateness in reporting. A patient contracting gonorrhea often does not realize that he is infected until the discharge is profuse, and during that time a spell of hard work will do much harm. Also, a number delay reporting to the medical officer in the hope that the discharge will disappear. Thus, of 101 epididymitis cases in the series of 500 acute cases, seventy were present on admission and likewise eight of the ten arithritis cases. Of the prostatitis cases, the exact number present on admission can not be stated, since routine examination of the prostate was not carried out until the end of the second week of treatment.

An analysis of the uncomplicated cases shows that 60 per cent. were under treatment thirty days or less, with an average of nineteen days. The average duration for the whole of the uncomplicated cases (278) was thirty-five days, or five weeks.

The complicated cases show clearly the importance of thorough treatment of the prostate, the cases of prostatitis requiring, on an average, ten days longer than those of arthritis, and twenty-two days longer than those of epididymitis. The longest cases of all were those in which acute prostatitis was allowed by acute epididymitis, this group forming 3 per cent. of the total. The average stay of all complicated cases was fifty-two days, or several days under two months.

It has from time to time been suggested, though never with adequate proof, that vaccines are dangerous in the acute stage, and lead to complications. If this were so it would have been expected that in this series of 500 acute cases, all treated from the start with big doses, a large proportion of complications would have developed, especially epididymitis and arithritis. This is not the case.

Of the 101 epididymitis cases seventy were present on admission, leaving thirty-one which developed out of 430 cases, or 7 per cent.

Of the ten arthritis cases eight were present on

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admission, leaving two which developed out of 490 cases, or less than 1 per cent.

The most remarkable feature of all is the exceptionally low percentage of relapses. Out of the 500 cases two only have occurred during a period of four months after completion of the series. Many of the patients left the hospital more than six months ago. This gives a relapse rate of less than 1 per cent. It is a very satisfactory proof of the value of vaccines as a test of cure, and although by omitting it the number of days under treatment could be reduced in many instances, the relapse rate would very soon counterbalance any gain. At the present time everything possible has to be done to minimize the number of relapses of gonorrhea cases, and this system has been found, in actual practice, to be far in advance of any other; whilst the number of days under treatment compared favorably with any known figures.

Captain Lumb also treated a series of acute cases with the *electro-chemical method of Russ.*[7]

Of twenty acute cases so treated one patient only, a mild case, was cured. In this instance twelve applications were given and no other treatment. In the remainder the discharge soon diminished, but the urine did not become entirely clear, and after three weeks' treatment vaccines were used. One of the twenty, a severe case, was practically unaffected after twelve applications. In others various solutions and current strengths were adopted, but with no more definite results. Undoubtedly this treatment has a beneficial influence on the urethritis in the acute stage, because the discharge and soreness diminish, but in these cases there was nothing to indicate that it could be considered curative.

Treatment of Gonorrhea in a Field Ambulance. A syringe, even in the hands of the surgeon, is unsafe; in the hands of the patient it is dangerous, says Lieut.-Col. Burke,[8] R. A. M. C. The syringe is bad treatment and the sooner it is relegated to the museums

(7) Practical Medicine Series, 1916, Vol. IX, p. 118.
(8) Lancet, May 19, 1917.

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as a relic of the dark ages of urology the better. No matter how careful one may be, one is always in danger of overcoming the resistance of the compressor urethrae muscle, forcing back some gonococcal material and extending and complicating an originally simple disease. The disease begins anteriorly; it should continue anteriorly. It should finish in the same place, and "leave not a wrack behind." By proper use of the Janet method this can be done; improvement is rapid, the relief of symptoms is almost immediate, and the cure is permanent.

Lieut.-Col. Burke was forced to extemporize a much modified Janet's lavage apparatus, as is shown in Figure 5. It was composed of a douche-can with a holding capacity of four pints. This was procured from No. 1 Field Surgical Pannier. Two separate 3-ft. lengths of rubber tubing were also culled from the same source. These were joined together by a vulcanite stopcock. One end of the tubing was fixed to the outlet of the reservoir; the other end was threaded through the stem of an enameled-iron filter funnel and finally finished off with a vulcanite enema-syringe nozzle, as is shown. The object of the filter funnel is, as in Janet's apparatus, to catch any backwash from the urethra and to protect the surgeon from being splashed with the returning solution. The solution used was potassium permanganate. No definite strength was adhered to, as the urethra gradually acquires a toleration to potassium permanganate. On the first day irrigation was commenced with the solution of a faint pink color, and this was gradually increased in strength each day.

The theory of the treatment is briefiy this. It is to be recognized that the great danger in all local treatment of gonorrhea is of infective material being carried past the barrier of the compressor urethra *and being left there.* This danger is realized as being inevitable, and so means are taken to wash out the whole urinary canal from the bladder to the meatus, and thus to ensure that every vestige of infective material be carried away. At the same time, the lavage solution is of such a nature as to render innocuous any of the organisms which may be present.

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The method is as follows. The patient having micturated (thus flushing out the urethra), he is placed lying on his back on a table, with his legs apart and his thighs slightly flexed. Between his thighs is placed a basin to catch the back-flow of solution from the urethra. The glans and prepuce are thoroughly cleansed, the douche-can is raised about 2 ft. above the patient's pelvis, an assistant turns on the stopcock, and a gentle stream of the irrigating solution is allowed to flow. The temperature of the solution is 104° F. The surgeon then inserts the nozzle, while the stream is flowing, into the urinary meatus, and the anterior

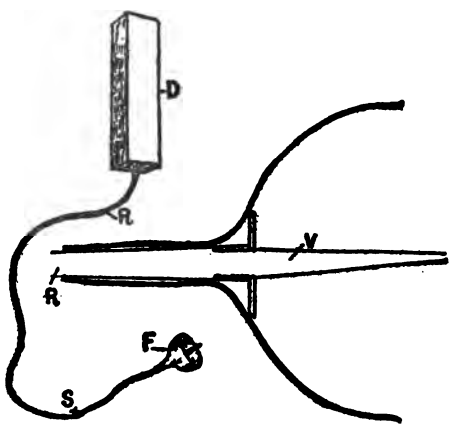

Fig. 5. Sketch of extemporised Janet's lavage apparatus, with a longitudinal section on a larger scale through the filter funnel showing the nozzle in position. D, douche can; R, rubber tubing; F, filter funnel; V, vulcanite nozzle; S, stopcock.

urethra is thoroughly washed out. An elevation of 2 ft. of the reservoir above the patient's pelvis is not sufficient to overcome the resistance of the normal compressor. The irrigation stream is kept at a steady flow, and by alternately inserting and withdrawing the nozzle from the meatus the anterior part of the urethra is thoroughly flushed with fresh solution. While not overcoming the compressor, the elevation of from 2 to 3 ft. is sufficient to cause a dilatation of the anterior

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urethra, to open up the crypts and lacunae, and to bathe them in permanganate solution, thus bringing every part of the urinary canal under the influence of the irrigating solution. If the disease be confined to the anterior urethra that ought to be sufficient. The point to realize is that there is no means of absolutely preventing relaxation of the compressor, therefore one has to suppose that in every case relaxation has taken place, and that it behooves one to take appropriate measures to prevent any damage. The reservoir is now raised to a height of 5 to 6 ft. and the stopcock is opened to its fullest extent. Experience has shown that this elevation is normally sufficient to overcome the compressor. The patient should be instructed to breathe easily and to attempt the act of micturition, thus relaxing the compressor, and the solution will be found to run into the bladder.

The treatment by the Janet method is more successful in rapidity of disappearance of symptoms than any other. In civil practice experience has shown that the gonococcus can be cleared from the urethra in three weeks by this method; and that there is no sequela. These results are even more important in soldiers on active service than in civil life; and even with the modified and extemporized apparatus used as described the results were almost perfect. Lastly, it is not beyond the resources of a field ambulance on active service to treat efficiently and cure cases of acute gonorrhea by the method of lavage.

A New Urethral Clamp. It is frequently found desirable to retain medicated fluids or jellies in the anterior urethra of the male over a prolonged interval. As it is rather tiresome for either the patient or the medical attendant to employ digital compression to the meatus urinarius for the required length of time, Walther[9] has devised a simple urethral clamp which answers the purpose for which it is designed (Fig. 6).

It is constructed of a single piece of finest quality steel wire 2 mm. thick, of figure-of-eight shape and with a strong grasp, and it measures 8 cm. long by 3.5 cm.

(9) Jour. Amer. Med. Ass'n., June 9, 1917.

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side. Finger-grips are conveniently placed, one on either side of the lower part of the clamp frame. The blades proper for compressing the meatus are each 2 cm. by 1 cm.; on their inner surfaces they have serrations which prevent slipping, once the clamp be prop-

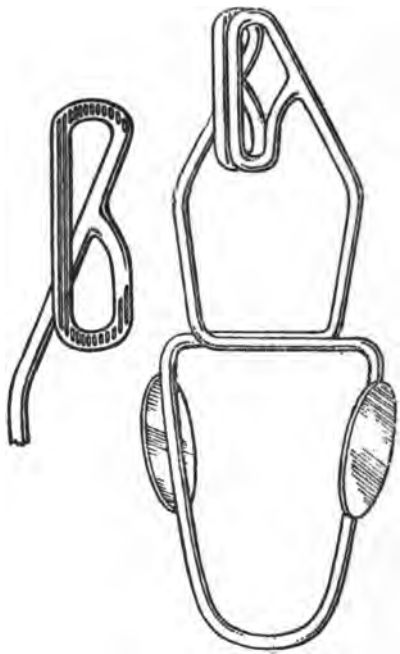

Fig. 6. Urethal clamp.

erly applied. The inner surface of one of these blades with serrations is shown, greatly enlarged, in the inset on the left of the illustration, so as to bring out its exact construction. The latter feature adds no little value to the merit of the instrument. The clamp can be easily sterilized, lasts indefinitely, and will stay where it is placed. Although the clamp has a very firm spring, the blades are so constructed that no pain is experienced in its application.

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SYPHILIS.

Syphilis in the State of Minnesota. Estimates made from the various surveys leads Irvine[1] to conclude that there are at least from fifteen to twenty millions of people in the United States infected with syphilis and that from 10 to 15 per cent. of the population of Minnesota, or from 200,000 to 300,000 people, are syphilitic.

In the University Hospital, where the Wassermann test is now done as a routine in almost all services, seven positives were found in one hundred consecutive tests, and the patients are not admitted primarily for syphilis.

In the out-patient clinic for syphilis there were 371 cases registered and under control (Oct. 1, 1916).

According to the report of the Social Service Department, during the months of April, May, and June, the average daily attendance on the Monday, Wednesday and Friday clinics for syphilis was twenty-six, with a maximum of forty-six. In May, the attendance for dermatology and syphilis was larger than in any other department. It was 807; and 597, or 74 per cent., were for syphilis. Thus, for the month of May, 13 per cent. of the total attendance in the Out-Patient Department was for syphilis; and this is without making allowance for patients registered in other departments, and not yet referred to the department.

Although a fair estimate of the prevalence of the disease in the state can be made, it is obviously impossible to draw any very definite conclusions as to what the disease actually costs the state. The legal value of a life in Minnesota is $7,500, if a person be accidentally killed; but who shall place a value upon lives needlessly lost through general paresis, tabes dorsalis, aortitis, apoplexy and arteriosclerosis? What might be the value of the hundreds of lives of stillborn babes if they had been born alive and healthy? What value shall we place upon the loss of eyes, and the partially lost brains of the hereditary luetics?

Blaisdell has recently made a study of syphilis in the family, and his figures are interesting in this connec-

(1) Journal-Lancet, April 1, 1917.

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tion. Thirty families formed a basis for the study. Less than ten per cent. of the husbands were healthy; twenty-eight out of thirty wives were infected; and the remaining two were probably infected. There were 132 definite pregnancies in the thirty families; only twenty-three resulted in healthy children, the majority of these being born before the infection entered the family. Of the fifty-three living children twenty-four, or 45 per cent., were definitely luetic; of the seventy-nine deaths fifty-nine, or 74 per cent., may be credited to syphilis; in all, the disease claims eighty-three, or 62 per cent., of the 132 pregnancies. This also demonstrates the high percentage of innocent infections.

There is, however, one source from which more definite conclusions of the cost of syphilis can be drawn and that it in public institutions. It is a well-established fact that this disease is responsible for the presence of a considerable number of their inmates. Surveys in various institutions have shown an average of at least 20 per cent. of positive Wassermanns. Out of the total number of institutions in Minnesota there are five where we would expect syphilis to be an important factor. These are the asylums at Rochester, St. Peter, Fergus Falls, Anoka, and Hastings. At only one of these institutions (Fergus Falls) are Wassermanns being taken as a routine, and there the admittances since Sept. 1, 1915, show 30 per cent. positive. The average of many surveys is proved to be 20 per cent., and this figure is used in making the following calculations: The 1916 report for the Board of Control is just now in the making, and these figures are not available; the figures given are from the report of July 31, 1914. According to this report there were in these institutions 5,247 inmates; therefore, on the basis of 20 per cent., 1,094 are syphilitic. The average cost *per capita per annum* in the five asylums was $158.93. From this it follows that $166,781.24 is about the sum of the taxpayer's money that goes to care for the syphilitic insane each year in Minnesota. A further point of interest is that most of these cases are general paretics; and, as a rule, paretics do not recover, so that most of this money is hopelessly spent so far as its being of any

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real assistance to these patients at this stage of their syphilis.

In a few states and cities, syphilis has already been recognized as a public-health problem, and campaigns have been started for its diagnosis, treatment, and control. New York and Boston are undoubtedly taking the lead in the campaign against venereal diseases. In New York, the work was begun in 1911, and in May, 1912, venereal diseases were made reportable. Laboratories were established for the diagnosis of syphilis and gonorrhea, services to be rendered free to physicians and institutions. In 1914, 42,415 Wassermann tests were made, and 21,155 cases of syphilis were reported. A so-called advisory clinic was also established. This clinic was advertised just as quack clinics are—by posters in public toilets and by space in the newspapers. Its purpose is to interview infected persons, and to direct them either to qualified private physicians, if the patients are able to pay, or to a proper clinic. During 1914, 1,427 patients patronized this service.

Several years ago, Massachusetts appropriated $4,000 to be used for laboratory purposes in connection with venereal diseases. This past spring the legislature appropriated $10,000 to be devoted to laboratory equipment and maintenance, research, and free salvarsan when necessary.

Vermont passed a law in 1913 making syphilis reportable, and furnishing laboratory service and treatment at cost. In Indiana, syphilis is included among infectious diseases. In Michigan it is reportable. In Florida, in 1913, syphilis was included among the diseases concerning which the state health board should issue educational bulletins. Kansas made syphilis reportable in 1913. Iowa passed a law making syphilis reportable in 1913, also providing a penalty for its transmission, as well as making the person liable for civil damage. In Louisiana and Wisconsin, syphilis is reportable. North Dakota, in 1913, passed a law preventing the marriage of infected persons, and providing a penalty for marrying such a person. In a number of cities, ordinances have been passed, and laboratory service is maintained;

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among these are New York, Boston, Cincinnati, Buffalo, Montclair, and Orange, N. J.

[Since June, 1917, syphilis, gonorrhea and chancroid have been reportable diseases in Chicago. The name of the patient is not reported unless he fail to return for treatment within the prescribed time. If he go to another physician, that physician must report the fact to the physician the patient has quitted.—EDITORS.]

Many people say it is useless to pass these laws, for syphilis can not be controlled; in answer to this the figures of the last report of the Massachusetts General Hospital are quoted: During the year 1915 there were 3,358 cases of syphilis under treatment. These patients made 18,063 visits to the hospital, and less than 10 per cent. of them were lost. By "lost" is meant a patient who had entered the hospital or was under treatment during the year, and had not reported to the clinic within a reasonable time in 1916—in other words, over 90 per cent. of these patients remain under control in 1916. The records at the University of Minnesota show that of 179 cases admitted during 1915, 72.6 per cent. were lost, that is, they were not carried into 1916. However, upon reorganization of the clinic with social service forty-seven patients were brought back, and the clinic has had the high attendance quoted previously, and now has very few lost cases.

Despite the widespread dissemination of syphilis in Minnesota there is no provision made to control the disease or to treat the early active cases. Irvine says that there is not a single law on the statue books of Minnesota making it possible to handle syphilis as any other infectious or contagious disease is handled. On account of lack of an appropriation, the State Board of Health is entirely unable to supply any laboratory service, such as is furnished for typhoid, tuberculosis and diphtheria. For the same reason nothing in the way of treatment can be furnished.

The State does not furnish a single bed in a single institution for the diagnosis, detention, or treatment of an infectious case of syphilis.

The nearest it comes to doing anything for syphilis is supporting the syphilis clinic along with the other

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clinics of the Out-Patient Department of the University Hospital. This clinic is, of course, primarily a teaching one, and the public-health phase of it is forced into a position of secondary importance.

A great deal more could be accomplished there if sufficient funds were available, but at present all patients must even pay for salvarsan, no matter how urgently it is needed, whether to save the eyes of a child innocently infected or quickly to clear up a highly infectious case that it may not be a source of danger to the community. The State, apparently, can well afford to furnish residence for the incurably syphilitic insane for a rather indefinite period, but can not afford to furnish treatment for early cases, even though it cost no more than 25 or 30 per cent. of one year's expense for an institutional inmate.

The Minneapolis City Hospital has no beds for syphilis, but occasionally an exception is made and a case is admitted, if it seems quite necessary. Syphilis is treated in the dispensary. Patients must pay for salvarsan if possible; if they can not and need it badly, it is furnished by some charity or by the hospital.

Beds for syphilis are available in the City and County Hospital in St. Paul; usually from twenty-five to thirty are devoted to skin and venereal diseases. Salvarsan must be paid for if possible; otherwise the hospital or some charity furnishes it to worthy and needy cases.

There is practically no bed available in private hospitals for contagious cases.

Thus it is seen that while Minnesota spends approximately from $150,000 to $175,000 each year for the care of individuals made dependent on account of this disease, practically nothing is done by way of prevention, although statistics of various observers demonstrate that with moderately good treatment only an extremely small percentage of cases will develop these dreaded sequelae. It can safely be said that practically every case of late syphilis, whether of the nervous system, the cardiovascular system, or of some internal organ, gives a history of either lack of treatment or of poor treatment.

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The Syphilis Problem Among Confined Criminals. Boudreau,[2] assistant prison physician at Auburn, N. Y., reports the result of his intensive examinations of the prisoners for the detection of syphilis.

Between May 4 and Dec. 1, 1915, 135 specimens of blood were sent to the laboratory, and of these sixty-nine showed 1+ to 4+ reactions, or a percentage of 51.11 per cent. positive and 48.85 per cent. negative.

Since Dec. 1, 1915, all individuals admitted have been subjected to the test unless they had previously been at Sing Sing. During the five months following there were 179 admissions, of which 47, or 16.8 per cent., showed positive reactions. During the fiscal year of 1914-1915, 1,025 new inmates were received in the prison. The admissions increase each year, but even at the above rate there will be at least 173 men (16.8 per cent.) admitted each year suffering from syphilis.

In addition, the test has been made on the whole population of the Women's Prison. One hundred and twenty-seven specimens were sent from there; of these, eighty-four were reported negative, and forty-three positive, or 33.8 per cent. positive. The total population averages about 110. There are, therefore, about thirty-eight female syphilitics in this prison at all times.

Statistics show that a large proportion of those who have had the infective organisms of syphilis in their systems for a number of years without showing frank clinical symptoms are potential paretics or tabetics. With this in mind, two tables were prepared which were intended to show concisely the physical findings in the forty-seven cases mentioned above as having positive Wassermanns, and also fifty cases which had negative Wassermanns.

Of the first series, with positive Wassermann: Thirty-eight, or 80.5 per cent., showed stigmata of degeneracy; twenty-seven, or 57.44 per cent., presented abnormalities of the alimentary system; thirty-four, or 70.21 per cent., presented abnormalities of the respiratory system, including the nasal passages; eleven, or 23.41 per cent., presented abnormalities of the circulatory system; twenty-seven, or 57.44 per cent., glandular enlargement,

(2) Med. Record, Dec. 2, 1916.

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including fourteen with epitrochlear glandular enlargement; twenty-six, or 55.32 per cent., presented defective vision; eleven, or 23.40 per cent., presented neurologic symptoms, such as dizziness, headaches, convulsions and paralysis; twenty had chancres over three years ago; eleven had chancres less than three years ago; thirty-one admitted chancres, but only eight showed scars; sixteen denied chancre, but three showed scars. Of the fifty showing negative Wassermanns: Thirty-nine, or 78 per cent., presented abnormalities of the alimentary system; forty-seven, or 94 per cent., presented abnormalities of the respiratory system; forty-seven, or 94 per cent., presented abnormalities of the circulatory system; twenty-eight, or 56 per cent., presented glandular enlargement, including six with epitrochlear enlargement; thirty, or 60 per cent., presented defective vision; four, or 8 per cent., presented neurologic symptoms; seven gave histories of chancre.

Comparison of these groups gives nothing that is conclusive, because the number of cases is too small and the difference in clinical findings too slight, but it is rather suggestive that 23 per cent. show neurologic symptoms in the first group and 8 per cent. in the second.

From the first group, the following conclusions can be drawn: 36 per cent. would have been overlooked if histories alone were considered; 42 per cent. would have been overlooked if glandular enlargement alone were considered; 76 per cent. would have been overlooked if scars alone were considered; 57 per cent. would have been overlooked if all physical findings alone were considered.

Of all of these forty-seven cases, none presented frank symptoms of tertiary involvement, and twenty suffered from the disease for over three years. Therefore, twenty, or 7.5 per cent. of all admissions, we may say are potential paretics or tabetics, or future wards of the State.

Granted that the State wishes to protect itself from this future expense, it should furnish, first the necessary money for treating these cases; second, a workable method for treating so many cases for at least two years;

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and third, medical men expert enough to administer the treatment thoroughly.

It is generally accepted that salvarsan or neosalvarsan is essential to proper treatment. At least five doses should be given. Salvarsan, when obtainable, costs $2.50 a dose. In conjunction with it, mercury should be administered intermittently until the cure is effected, but the expense of this is slight. Finally, the iodide of potassium must also be given at intervals to make the mercury effective, and this is at present $6 a pound. It will require about one pound for each patient a year. Summed up, then, the minimum cost *per capita* a year would be:

Salvarsan	$12.50
Mercury	7.50
Potassium iodide	6.00
	$26.00
And for 175 patients	$4,550.00

The expense the second year will be nearly doubled, for 175 new sufferers will be added each year.

It is easy to see that the problem of treating so many patients over a period of at least two years, many of whom, as shown by past experience, are delinquent if left to themselves, is a big one. At the rate of 175 a year there would be an average of fourteen a month to be treated, necessitating the administration of seveny-five doses of salvarsan a month, to say nothing of the supervision of the iodide treatment and the injections of mercury. This is special work in a class with special treatments of the eye, ear, nose and throat, or the work of the other specialties, and can not be expected of the regular prison physicians.

Therefore, to fill the third requirement, a trained syphilologist should be furnished.

Syphilis in Toulouse in War Time. There has been much talk about the marked increase in the number of syphilitics since the beginning of the war, but there have been few figures available. Audry,[8] chief of the clinic at the University of Toulouse, gives the figures

(8) Ann. derm. et syph., 1917, p. 419.

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body. While a positive Wassermann reaction would be of great assistance, it would not, of course, prove that any special lesions were specific. The reaction is, furthermore, negative in a certain proportion of cases, especially those that occur ten or even twenty years or more after infection.

Previous to the introduction of salvarsan, the treatment of palmar syphilides was invariably difficult, the lesions in some cases disappearing only after the most vigorous use of mercury by inunctions or injections. Some cases absolutely refuse to clear up after a long series of salicylate of mercury injections. With salvarsan or allied drugs (neosalvarsan, arsenobenzol) the treatment is generally recognized to be highly satisfactory and often most brilliant. It is now a common experience to see a palmar syphilide, that may have existed for years, disappear completely in from one to four weeks after a single injection of salvarsan.

Multiple Chancres of the Lip. This case of double extragenital infection with *Spirochaeta pallida,* reported by E. Zeisler,[7] is of interest because of the rarity of extragenital chancres in the colored race, and because of the simultaneous inoculation of the lower lip at two symmetrical positions, thus producing a double chancre and a bilateral submaxillary bubo.

The patient was a colored woman, 19 years old. There were two cherry-sized protuberant masses on the lower lip, symmetrically placed on either side of the midline, of approximately equal size, and each one about three-fourths inch in diameter and extending from the cutaneous edge across the vermilion portion of the lip. Both nodules were indurated, and the surface was excoriated, covered with reddish-brown crusts, and exuded a bloody serum on pressure. The entire lower lip was somewhat edematous; the upper lip was unchanged. Bilateral submaxillary enlarged glands were present. The glands on the right side of the neck were somewhat larger than those on the left. There was generalized adenopathy, with marked enlargement of the posterior cervical and occipital chains. The mouth showed an angina involving the pillars and tonsils, but no mucous

(7) Jour. Amer. Med. Ass'n., May 26, 1917.

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patch. A beginning typical macular eruption was faintly visible on the chest and the abdomen (see Plate XII).

Chancres of the lip are the most frequent form of extragenital infection. Cole's recent report of sixty-one extragenital primary lesions includes forty-three lip cases, of which thirty-two were on the lower and seven on the upper lip. Bulkley, out of a total of 9,058 extragenital chancres, found that lip infections constituted 20 per cent. (1,810 cases). In his private practice he reports fifty lip chancres out of 113 extragenital lesions. Fournier found that extragenital lesions comprised 7 per cent. of all chancres, and that there were 567 lip cases out of a total of 1,124. These statistics are sufficient to show that the lip is a frequent site of infection with *Spirochaeta pallida.*

It is stated that lip chancres occur more commonly in women than in men, and affect the lower lip in preference to the upper lip. Gaucher and Milian in 1893 pointed out that the roseola appears earlier in lip chancres, probably because of the greater vascularity of the lip as regards both vessels and lymphatics. The initial lesion on the lip is usually single, and is frequently of such size as to push out the lip prominently and disfigure the face.

Two Men Infected by the Same Woman. Two young soldiers of similar physique and of the same age, with chancres, were seen by Lévy-Bing.[8] They had been exposed, the one immediately after the other, to the same woman. Both lesions appeared in exactly ten days, and on exactly the same area on the penis.

Primary Syphilis of the Rectum. As primary syphilis of the rectum is rare, a case reported by Jost and Gradwohl[9] is of interest.

The figures of Fournier and those of Gradwohl show that cephalic chancres constitute perhaps 75 per cent. of extragenital chancres. Most of them occur upon the lips, indicating that transmission is by kissing. As for anal chancres, they are observed in women more than in men, usually a *proepostera venere;* in man this is always the case. They are classified as anal, peri-anal, and rec-

(8) Ann. des. mal. vén., 1917, p. 149.
(9) New York Med. Jour., Nov. 4, 1916.

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tal. It is to the latter class that the present case belongs. The peri-anal chancre resembles a fissure in appearance. The edges are everted and the base is indurated. Its appearance may be compared to an anal fissure that has been cauterized. The anal chancre may be intra-anal and may not be seen unless the anal opening be stretched. According to Fournier, it appears as a mere red erosion, composed of two segments which fold upon each other like the leaves of a book. The true rectal chancre, which is very rare, is situated from 3 to 4 cm. above the sphincter. Bogrow observed one as high up as 8 cm. Often it is discovered only in a patient with already pronounced secondaries, where after searching in vain for an initial lesion we are told by the patient that he has had pain upon defecation and that the discharges are colored with blood. By speculum examination the lesion is then discovered.

There always is an accompanying lymphadenopathy in the external inguinal glands in these cases, as was the case with this patient. It must be remembered that inguinal gland enlargement occurs in these cases through the anastomoses between the lymphatics in the concavity of the sacrum and those in the groin.

The patient was a French Jew waiter and confessed that he had exposed himself to the sexual attack of a sodomist.

Involvement of the Bones and Joints in Early Syphilis. The conception that syphilis in the early weeks and months of the infection attacks for the most part the superficial structures, and that the severe visceropathies and syphilitic disease of the bones and joints belong rather to the group known as the late sequelae, is without doubt due to the fact that there has been little opportunity for studying the disease in its incipiency, as is possible with other diseases. It is only within very recent times that the hospital bed has become available for the freshly infected syphilitic. With the increased facilities for study of the disease early in its course it has become more and more apparent that all of the deeper structures are affected early in the course of the disease.

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During the past four years Wile and Senear[1] have been enabled at the University of Michigan clinic to give particular attention to such phases of early syphilis as have not been previously studied. In all their cases they paid particular attention to the involvement of the nervous system, general health of the individual, the question of loss of weight, the involvement of the spleen and liver, and the involvement of the bony structures.

That the bony structures, including also the articulations, are involved as late or so-called tertiary sequelae is of course well known. A surprisingly small literature, however, exists dealing with the involvement of the bones and joints as part of the early manifestations of syphilitic infection.

During the past two years the authors studied, with particular reference to early bone and joint involvement, 165 cases of syphilis in the primary and secondary periods. In all sixty of the 165 cases were found to have symptoms or objective findings referable to the pathology of the osseous system.

Of the sixty cases in which bone or joint involvement was found, thirty-six showed some definite constitutional disturbance due to their syphilis. Thus in eighteen cases the general health was severely affected, as attested by severe anemia, debility, and a great loss of weight. Eight cases showed a mild involvement of the general health disturbance, and the remaining 10 cases showed only a slight loss of weight and a mild degree of anorexia. The twenty-four remaining individuals were entirely devoid of constitutional symptoms.

The analysis of the eruptive phenomena associated with bone involvement showed no apparent relation between the two to exist. All types of syphilides in about an equal proportion were found to exist with the bone manifestations.

In thirty-one of the sixty positive cases in the series careful neurologic examination was made. Of these, fourteen gave positive findings of the spinal fluid, together with associated neurologic findings, whereas seventeen were found to be uninvolved. Forty-five per

(1) Amer. Jour. Med. Sci., November, 1916.

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cent., therefore, of the cases in which bone and joint involvement was present were cases also of neural syphilis. A previous investigation of all cases of secondary syphilis in this clinic with reference to early involvement of the central nervous system showed 70 per cent. of the cases involved. The marked difference between the figures in all cases of secondary syphilis and those which showed bone and joint involvement suggests an inverse ratio between the involvement of these two systems.

In about 30 per cent. of these cases in which the bones and joints were involved, definite splenic enlargement could be demonstrated.

With regard to the development of the bone and joint manifestations, it is interesting to note that of the sixty cases, only three could possibly have been associated with definite traumata. In fifty-seven the involvement seemed to be entirely spontaneous. This is in striking contrast to the development of the bone and joint manifestation in the later stages of the disease, in which the element of trauma is an all-important factor in the development of the pathology.

In the vast majority of the bone cases, the patients had received little or indifferent treatment, and only one or two had received efficient treatment.

The symptomatology of the cases is as follows: twenty-seven cases showed involvement of the bones only; in twenty-one the joints were affected independently; in the remaining twelve cases the bones and joints were involved together.

In all but one case in which the bones were involved more or less pain was present. This varied from a dull intermittent pain described by some patients as a "dragging sensation" to the most exquisite, sharply localized tenderness. For the most part the pain was nocturnal in character and was relieved somewhat by exercise.

Arthralgia was the most common finding referable to the articulations. It was present in seventeen of twenty-one cases studied. The pain, as in the cases of the bones, was for the most part nocturnal, and was also relieved by exercise. In the order of frequency the ankles, the metatarsophalangeal joints and the

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elbows were affected, and in one case the elbow and shoulder joint of the same side were affected. Pressure on such joints was always followed by sharp pain. In all of the arthropathies only five cases were shown to have objective signs. In one case the knee showed a distinct, symmetrical swelling, in a second the hip-joint, in a third the shoulders were the sites of visible tumescence. Definite hydrarthrosis was present in two cases; both the knees were affected in one and both ankles in the second. In one case there was marked swelling of both knees without any subjective disturbance. In all of the cases studied prompt amelioration took place as soon as efficient treatment had been begun.

The periosteal node and early arthralgia may be looked upon as relatively superficial syphilides and rapidly amenable to treatment. The involvement of the medulla of the bone, however, must be regarded much in the same light as a severe visceral syphilide comparable, perhaps to the involvement of the spleen. It is not at all unlikely that spirochetal "rests" occur in the marrow of the long bones from such early implantation. Such rests may well serve as distributing foci of the later sequelae, not only in the bones themselves, but possibly such foci serve as depots from which, under the influence of either trauma or other factors, the circulation is recharged with spirochetes.

Syphilis as a Cause of Chronic Urticaria. Chronic urticaria is extremely rebellious to treatment and a cause of great distress to the patient. The cause is usually obscure and in many cases can not be determined. In not a few cases focal infection is either the causal or contributing factor. Haase states that in many of his cases he has found malaria and that the disease will disappear upon the proper administration of quinine. Wolff has shown that it may occur in connection with hydatid cysts.

Hazen[2] saw a dispensary patient, a negress who had been formerly treated for late syphilis, and who reappeared with a severe case of chronic urticaria that had lasted for almost six months. The Wassermann reaction proved to be strongly positive, and injections of mer-

(2) Amer. Jour. Syphilis, October, 1917.

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cury were at once begun, with the result that the urticaria disappeared in ten days. Negro-like she promptly stopped treatment, and in four weeks the urticaria reappeared, and again the administration of mercury stopped it promptly. Shortly thereafter three other similar patients were seen. Hazen then began to make routine Wassermann examination of all patients with chronic urticaria, and to date has a record of eighty-nine cases, with twenty-eight positive serum reactions. This is much higher than the routine positive Wassermann results in other patients, either in the wards or the clinics, where the average positive findings are about 20 per cent. He was able to follow twenty-three of the twenty-eight patients, and all were relieved of their urticaria by either mercury or salvarsan. In seven cases mercury was given to Wassermann-free patients suffering from chronic urticaria and in no instance was either the itching or the eruption affected.

In private practice, he tested eighteen patients who were suffering from chronic urticaria for a positive complement fixation, and in not a single instance could a positive result be obtained, hence it is probable that it is chiefly among the hospital and dispensary classes that syphilis will be found to be the cause of chronic urticaria.

Arterial Hypertension and Syphilis. The part played by syphilis in the production of arterial hypertension has been variously stated. In a study of a series of 124 patients with arterial hypertension, J. S. McLester[3] found twenty-one cases manifesting a positive Wassermann. In view of his figures, it is difficult to credit some of the more extravagant statements, such as that by Stoll, that 50 per cent. of hypertension patients have syphilis. The fact that Stoll based his statement on results obtained with the luetin test may explain his figures. We are familiar with the general statement that syphilis is the chief producer of arterial disease, and we are accustomed to look upon arteriosclerosis as a cause of hypertension, but herein are two fallacies. While syphilis does produce an enormous amount of disease of the ascending aorta, of the coronary arteries

(3) Amer. Jour. Syphilis, October, 1917.

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and of other groups of vessels, the statement that it is the most frequent cause of widespread general arteriosclerosis may be doubtful. And, too, our views regarding the mutual relationship of arterial disease and hypertension are undergoing a change, for there is good reason for believing that, in many if not in most instances, the hypertension precedes rather than follows the arteriosclerosis.

[Shamberg is of the opinion that the mercurial treatment is more frequently the cause of hypertension than the disease for which it is administered. Mercury is, of course, highly irritating to the kidneys and by the production of a chronic nephritis may lead to hypertension. McLester found both albumin and casts in 50 per cent. of this series of cases.—EDITORS.]

Effect of Soap on Treponema Pallidum. The results of some experiments of Major Reasoner,[4] M. C., U. S. A., were convincing that the organisms of syphilis will not live in the presence of a solution of soap of even a considerable degree of dilution, and that a lather, such as used in shaving, is sufficient, when brought in contact, to cause their immediate death. It is possible that some of the initial lesions on the face which have been ascribed to the barber may have been transmitted by a towel wet only in water, which towel has served to convey the infection from another patron or perhaps the barber himself. Another possibility is that the person, immediately after shaving, and while still having many minute abrasions on the face, has submitted himself to osculatory salutes from an infected prostitute. It would seem that a solution of soap or lather, such as is used in shaving, should have some value as a prophylactic measure against syphilis, but, probably for several reasons, not equivalent to the mercurial preparations now in use.

DIAGNOSTIC METHODS.

Wassermann Tests Done During 1916 in the Philadelphia General Hospital. Rosenberger[5] reports the results of 5,106 Wassermann tests done in this institu-

(4) Jour. Amer. Med. Ass'n., April 14, 1917.
(5) New York Med. Jour., June 30, 1917.

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tion. Of these tests 4,430 were performed with the blood serum, and 676 with the spinal fluid. The ordinary routine technique was used, with three antigens—alcohol extract of syphilitic liver, acetone-insoluble lipoid, and cholesterolized alcoholic extract of beef heart. Taking the total number of all specimens of blood submitted there was a general average of 27.4 per cent. positive. The latter figure is accentuated by the fact that a large number of specimens were from the insane department. In 133, positive reactions were obtained with the cholesterolized antigen alone, and in looking up the histories of these cases, it was found that a certain number gave more or less definite syphilitic histories. Unfortunately, in a very large number of the total cases, no diagnosis was made at the time the serum was sent to the laboratory, and no diagnosis of a specific nature was found, even after looking up the history sheet in the record room.

Among the specimens of blood serum received for examination, fully 100 were anticomplementary and were not included in this report. From the men's medical ward, where it is almost routine, 1,097 were examined, and of this number 259, or 23.5 per cent., were positive. From the women's medical ward, 273 examinations were made, and of this number 103 were positive, or 37.7 per cent. In 273 submitted from the men's and women's surgical wards, including eye, orthopedic and dental, ninety-two were positive, or 33.3 per cent. The cases in the psychopathic wards included all types of mental cases under observation, toxemias of pregnancy, manias, dementias, including praecox, paresis, and paranoia, and traumatic and alcoholic confusional insanities. In all, 906 specimens of blood were submitted and of these 198 were positive, or 21.8 per cent. Of the 432 specimens obtained from the nervous wards, 103 gave a positive reaction, or 23.8 per cent. Gynecologic cases numbered sixty-nine, of which twenty were positive, or 26 per cent., and of fifty-eight from the men's venereal ward forty-five were positive, or 75.8 per cent.; 278 were examined from the women's venereal ward and 127 were positive, or 45.7 per cent.

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An interesting series was also obtained from the wards of the tuberculosis department. Of these 291 specimens were examined, ninety-eight, or 33.6 per cent., of which gave a positive reaction. From the children's department there were only fifty-six examined, of whom eight, or 14.2 per cent., were positive. Maternity cases numbered 136, of which ten were positive, or 7.3 per cent. In 561 specimens from the insane department, only 154, or 27.4 per cent., gave a positive reaction.

A *résumé* of the examinations of the spinal fluid showed that of 676 studied, 151 were positive, or an average of 22.2 per cent. From the men's medical ward, of 258 tested, only thirty-one were positive; from the women's medical ward, thirty-six, of whom seven were positive; of seventy-one insane cases, forty-one were positive; of 107 specimens from the psychopathic wards thirty-seven were positive. Of 139 cases from the nervous wards, thirty were positive, while of twenty-eight specimens from the surgical wards two reacted positively, and of sixteen from the tuberculosis wards three gave a positive reaction. Of the 133 cases giving a positive reaction with the cholesterolized antigen and negative results with the other two antigens were eight male cases of tuberculosis. Only one gave a history of venereal disease—a chancre ten years previously.

From the men's nervous ward there were twelve cases, and of these 50 per cent. gave a history of venereal disease; four gave a history of chancre; one a right-sided hemiplegia, and the sixth was an adult who had been unable to walk since his second year and whose father has tabes dorsalis. No history was available in the other six cases.

From the men's psychopathic ward, sixteen cases were tested, and of these ten were diagnosed as paresis; one as hemiplegia; one mania; one as cerebrospinal syphilis; one alcoholic confusion, and in two no history was obtainable. In the series from the women's psychopathic ward only three cases were studied: one dementia praecox, one paresis, and one alcoholic psychosis. From the insane department, twenty-two cases gave a positive reaction, three were paresis; four, dementia praecox; one, cerebrospinal syphilis; three, senile dementia;

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one, depressive senile psychosis. While a positive history was not given in all these instances, yet the record from a social standpoint would indicate a specific history.

From the women's medical wards eleven gave a positive reaction. In not one was a venereal history obtainable, but the clinical diagnosis and social history indicated that venereal infection had been present.

From the men's medical ward, thirty-two cases gave a positive cholesterolized antigen reaction, and of these only five gave positive syphilitic history. Two, while denying syphilis, gave two positive findings on different occasions; one gave a history of gonorrhea and persistent headaches; one, denying infection, was diagnosed as cerebrospinal syphilis; in eleven no venereal history was admitted, and in twelve no history of any kind was obtained.

From the gynecologic ward nine cases were encountered, and only one gave a positive venereal history. However, one case was diagnosed as syphilis; another patient had had two miscarriages; another had two still births; and one, aged seventeen, with gonorrhea, who denied all venereal history, gave birth to a child whose blood gave a positive reaction.

Of three cases from the eye ward giving a positive reaction, in two no history was available, and in the third a diagnosis of syphilitic iritis was made, and this condition cleared up on antisyphilitic treatment. From the women's surgical ward one patient, 58 years old, denied syphilitic history, but had a long-continued ulceration of the leg. Of two other cases, one in a patient aged 55 years, was diagnosed as syphilitic leg ulcer, although he denied syphilitic history; and the other gave a history of a chancre twenty-one years previously.

Routine Wassermann Examinations for Obstetric and Gynecologic Patients. The diagnosis of syphilis in women is more difficult than in men so far as the recognition of the initial lesion of the disease is concerned. Even when the chancre is situated on the external female genitals it may escape notice or be judged insignificant by both patient and physician, because in women

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the chancre is smaller and not so indurated as is the initial lesion in the male. Furthermore, the scar of the primary lesion in women is less marked and therefore less recognizable than in men.

As a consequence, syphilitic infection in women is either overlooked or passed over slightly by the gynecologist, or treated by the obstetrician in a haphazard manner, when the evidence of the disease is unmistakable in either mother or fetus.

Peterson[6] gives the results of the routine Wassermann examination and intensive search for syphilis in all obstetric and gynecologic patients at the University of Michigan.

It is generally believed that syphilis is more common among men than among women. Pusey and Pollitzer, from the result of their observations, believe lues to be two or three times more common in men than in women. Hubert, on the other hand, from careful histories of possible luetic infection, combined with routine Wassermann tests, found in between 8,000 and 9,000 patients examined that the proportion of syphilitics among the women was 0.5 per cent. higher than among the male patients. It will require some years of careful statistical study of syphilis with modern diagnostic methods before we will be in a position to know definitely in which sex the disease is more prevalent. It may well be that many cases in women have been overlooked for reasons already mentioned and because women, far more than men, shrink from being examined for syphilis. Routine blood examinations where the patient remains in ignorance of the purpose of such examination may very well in the next few years change our opinions regarding the frequency with which the two sexes are affected.

In a report previously made it was found that there were eighteen undoubted cases of lues in 381 obstetric patients examined, or 4.7 per cent. It was stated at the time that subsequent reports might show a decidedly higher proportion of syphilitics in this clinic and that this is true is shown by the examination of ninety-six additional obstetric patients, among whom there were

(6) Amer. Jour. Syph., January, 1917.

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ten undoubted cases of syphilis, or a percentage of 10.4—over twice as high a percentage as in the first series. However, percentages based upon such a small number of cases are relatively of very little value. A better idea of the prevalence of syphilis in obstetric patients of this kind may be obtained by adding the two together. Thus in 477 obstetric patients there were twenty-eight undoubted cases of syphilis, or 5.8 per cent. While this probably is a higher percentage than will be found in the average private obstetric practice, the proportion would not probably be much higher if the same careful tests were made in an equal number of private patients, because the patients making up this clinic are not unduly exposed to syphilis, since they are not prostitutes, but country girls, waitresses, domestics, and stenographers.

In the twenty-eight syphilitics out of the 477 patients examined there were only twelve who gave positive histories of infection. Eight out of these twelve patients gave a 4 plus Wassermann reaction, one, a 2 plus, while three were doubtful, or plus minus. Such findings show the necessity of not limiting the Wassermann examinations to the obstetric patients who give histories of syphilitic infection, but to look forward to the time when every pregnant woman will have her blood tested, just as today every careful practitioner insists on frequent examinations of the urine.

Only eleven of the twenty-eight syphilitic patients, or less than half, showed evidence of the disease even after the most careful physical examination. Naturally these patients showed a large number of 4 plus Wassermanns, eight out of the eleven; whereas of the other three, one gave a 4 plus, two being plus minus or doubtful. However, most interest centers on the seventeen cases in which the physical signs were doubtful, the Wassermann tests were 4 plus, while of the remaining thirteen cases of syphilis, but without physical manifestations of the disease, seven gave 4 plus Wassermanns, one a 3 plus, two 1 plus, whereas the Wasserman was negative in three, the diagnosis being made from other circumstances connected with the cases.

Turning now from the obstetric to the gynecologic

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side of the problem of syphilitic infection in women, we see even greater confusion and lack of accurate diagnosis.

Syphilis may give rise to organic lesions in any part of the female generative tract, just as any organ in the body may be similarly affected. It is a curious fact, however, that until recently very little attention has been given to local syphilitic changes in the female generative organs, exclusive of the parts that are open to inspection, such as the vulva, vagina and cervix.

It is well to keep in mind two facts: (1) that many functional disturbances in women, supposedly due to derangements of the genital organs, may be due to an unsuspected luetic infection; (2) that gynecologic patients who fail to recover their health after operations upon the generative tract may be suffering from a serious general disease of far more importance than the local lesions for which the operations were performed. When the diagnosis of syphilis depended on the results of physical examination combined with careful history of exposure and subsequent symptoms, there was some excuse for the practitioner's failure to recognize the disease. There is no such excuse now that we can avail ourselves of the Wassermann test.

In the author's series of 606 gynecologic patients there were fifty syphilitic, or 8.2 per cent. Only twenty out of fifty luetic patients gave a history of infection. In many of the cases, both when there was a history of infection and when this was lacking, physical examination in the gynecologic clinic failed to arouse suspicion of the presence of syphilis. Additional evidence of lues was found by the syphilologist, but that was to be expected. The point to be emphasized is that the same careful physical examinations have been made in this particular clinic for years with only an occasional patient suspected of being luetic. When, however, such examinations are reinforced by routine Wassermann examinations, nearly 10 per cent. of the patients are found syphilitic and are sent to the Department of Syphilology for a confirmatory diagnosis and treatment. This is due almost entirely to routine Wassermann examinations. Granted that in certain cases such exam-

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inations are unreliable, this is not true in the great majority of cases. So great a help has the Wassermann examination proved in the public clinic that arrangements are being made to have routine Wassermanns made on all patients in the private clinic. Hereafter, such examinations will be as much a part of the regular pre-operative routine as the careful examination of the urine.

Wassermann Test in Surgery. With the introduction of the Wassermann test as a laboratory procedure, it was the custom of Major T. L. Rhoads,[7] M. C., U. S. Army, to request a blood examination in surgical cases only in such patients as gave a history of infection, or of past symptoms, or of suspicious lesions which might prove to be syphilitic. It was not long, however, before it was discovered that such investigation did not include all syphilitic cases that came under his care. It was found, for example, that certain slow-mending fractures gave serologic positive findings and these improved under antiluetic treatment; also that some cases of nephritis which were under treatment in preparation for surgical operation in other regions, like hernia and appendicitis, gave positive Wassermann tests and cleared up under salvarsan and mercury. Certain cases of diabetes with surgical requirements gave a positive test and responded to antisyphilitic treatment before operation was performed.

Major Rhoads therefore began to use the Wassermann test as a routine examination in all surgical cases. The result of this routine method has been invaluable in reaching diagnosis, both in obscure conditions and in cases in which lesions might likely be ascribed to other causes. There are, for example, under treatment in the surgical service of the hospital, several cases of syphilitic arthritis that were sent in as cases of rheumatism; a case of ascites that was sent for a Talma operation; a case of suspected amebic dysentery, and a case of necrosis of the tibia, in all of which the patients gave strong positive Wassermanns, and are undergoing antisyphilitic treatment. Even in cases of traumata of all kinds, including gunshot wounds, the Wassermann

(7) Amer. Jour. Syph., April 1917.

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test is not disregarded, and proper treatment following a positive report from the laboratory has influenced the course of healing.

Evidence of Syphilis in Subnormal Children. The authorities having charge of the children in the open-air schools of the city of St. Louis asked, with the full consent of the Department of Hygiene of the Board of Education, that certain examinations be made of the children attending these schools at the Dispensary of the St. Louis University School of Medicine. The Wassermann reactions were done and are here reported by C. D. Johnson.[8]

These open-air schools were arranged for children suffering from anemia and malnutrition of apparently unknown origin. The general impression was that these schools were maintained for the tuberculous and those of a tuberculous diathesis, and in the earlier periods when these schools were first opened some of the school medical inspectors selected only children of a tuberculous diathesis. A few children with a definite heart lesion were also admitted. Later, it became the policy to exclude cases with definite lesions of any kind, and anemia and malnutrition became the chief requisites for admission.

The children are examined carefully and thoroughly at regular intervals by the physicians of the open-air schools. They have been examined by various physicians in the dispensary of the St. Louis University, and also in other clinics. In only a few cases were any definite diagnoses made except of anemia and malnutrition, and in those few cases there was a difference of opinion among the clinicians who made the examinations.

Of the 224 cases over 33 per cent. showed a positive Wassermann (either a three or four plus). The author feels justified in considering these children as congenital syphilitics, especially when there are even slight clinical evidences of lues. It was found that approximately an additional 23 per cent. of these children showed a one or two plus Wassermann.

Latent Syphilis in the Canal Zone. Further evidence showing the value of routine Wassermann tests in hos-

(8) Amer. Jour. Syph., July, 1917.

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pital and dispensary cases is offered by the work of Captain Qualls,[9] M. C., U. S. A., at Ancon Hospital.

From a total of 1,198 colored surgical patients, 908 showed no evidence of syphilis nor did they give a history suggestive of the disease; 297 showed active evidence of syphilis or gave histories indicating previous syphilitic infection. The Wassermann test survey showed 23.7 per cent. of the non-suspects to be syphilitic, and 36.7 per cent. of the suspects to be syphilitic. A grand total syphilitic infection of 27 per cent. exists among all colored employees admitted to the surgical wards.

The latent syphilitic infection among colored male employees in the Canal Zone is exceedingly high; 23.7 per cent., as compared with the white employees showing 2.3 per cent. The total syphilitic infection among the white surgical patients was found to be 15 per cent.

It may be argued by some that a routine blood Wassermann, if positive, will tend to discourage a thorough physical examination and thereby result in treatment only of the disease without knowledge of the location of the disease, the condition of the patient, or the presence of other diseases. Such might apply to one not interested, or one with haphazard methods. To the zealous worker, however, the persistent positive blood Wassermann will be a definite indicator of an active pathologic process, and will in some instances even in clinically inactive syphilis, result in its location.

[There are two sources of error constantly creeping into routine Wassermann tests. One is the assumption on the part of the unskilled clinician that every pathologic process in a patient with a positive Wassermann is syphilitic and the other is that if the Wassermann be negative the lesion is, therefore, not syphilitic. The fault, however, is with the clinician and not with the routine Wassermann.—EDITORS.]

There is a large class of cases of latent syphilis of great importance, which will be missed by routine blood Wassermann tests. These are the cases of latent cerebrospinal syphilis. The great value of the examination

(9) Amer. Jour. Syph., October, 1917.

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of the cerebrospinal fluid in such cases has become increasingly apparent.

One Thousand Wassermann Reactions. A tabulation of 1,000 Wassermann reactions by J. M. Ladd[1] sheds some light on the percentage of the population infected with syphilis. These reactions were made while the writer was in the laboratories of the Casualty and Washington (D. C.) Asylum Hospitals.

1. The dispensary patients comprised 42.50 per cent. of the 1,000 cases.

	Per Cent.
Reaction negative (—)	52.80
Reaction plus minus (+ —)	11.00
Reaction plus (+)	10.70
Reaction double plus (+ +)	25.50
	100.00—425 patients

Of this number of patients, 68.80 per cent. were white and 31.20 per cent. were colored.

In the 25.50 per cent. of double plus reactions, 14.60 per cent. were colored and 10.90 per cent. white.

In the 52.80 per cent. of negative reactions, 29.80 per cent. were white, 23 per cent. were colored.

In the remaining 21.70 per cent. of plus and plus minus reactions, 13.90 per cent. were white and 7.80 per cent. colored.

In those patients in whom a diagnosis of lues had been made, 43.70 per cent. gave a positive reaction.

2. Patients in the wards of George Washington University Hospital, comprising 44.90 per cent. of 1,000 cases.

	Per Cent.
Reaction negative (—)	71.20
Reaction plus minus (+ —)	12.00
Reaction plus (+)	6.40
Reaction double plus (+ +)	10.40
	100.00—449 patients

Of the 449 patients, 43 per cent. were female white and 57 per cent. male white; 3.60 per cent. of the positive results were female white and 6.80 per cent. male white.

(1) New York Med. Jour., Nov. 11, 1916.

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3. In the private cases of the hospital and in outside practice (12.60 per cent. of the total).

	Per Cent.
Reaction negative (—)	62.50
Reaction plus minus (+ —)	19.27
Reaction plus (+)	4.13
Reaction double plus (+ +)	14.10
	100.00—126 patients

Of the 62.50 per cent. of negative reactions, 37 per cent. were white females and 33 per cent. white males.

Of the plus and plus minus reactions, there were 48.20 per cent. under treatment.

The foregoing figures show that the total population (all stations of life included) would give the following percentage:

	Per Cent.
Reactions plus plus are found in	17.38
Reactions minus are found in	62.09
Reactions plus or plus minus are found in	20.53
	100.00

A comparative study of the two races shows that the percentage of plus and plus minus reactions in the dispensary practice was 6.10 per cent. greater in the white population than in the colored, and in seeking a reason for the proportional increase, Ladd comes to the conclusion that the white race has more faithfully taken the advise of clinicians, and pursued continuous treatment at the dispensary.

Wassermann Reaction Investigated by Group Study Methods. The material in this paper by E. V. Knapp[2] is based on a review of the records of 400 cases studied routinely by the diagnostic section of St. Luke's Hospital, San Francisco. Nearly all these patients belonged to the middle classes and were, for the most part, chronically ill. Each case was under observation in the hospital on an average of 4.8 days. By the end of this time all the clinical procedures were completed and recorded. The study of each case consisted of a history,

(2) Amer. Jour. Syph., October, 1917.

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physical examinations in eleven departments of medicine, and laboratory examinations, including the Wassermann, in all but six.

Intensive study of the 400 cases showed that men are five times more frequently syphilitic than women; that the central nervous system leaves demonstrable traces of the disease in 50 per cent. of the cases; that most of the cerebrospinal syphilis cases are in the male division; that the most important single method of examination for syphilis is the physical examination, the Wassermann second and the history least. The most convincing clinical diagnosis is when physical examination, Wassermann and history are all positive, the next in importance when two are positive and one negative, and the least where but one gives positive evidence.

Post-Mortem Wassermann Reactions. The diagnosis value of the Wassermann test for syphilis performed on sera from human blood taken post-mortem has been the subject of investigation and discussion for the last ten years. Practically all published reports on the work have been made in Germany. The first to carry out this research concluded that the Wassermann reaction gave reliable results when done on post-mortem blood and that the results confirmed the prevailing comprehension of fibrous meso-arteritis and aneurysm of the aorta, as syphilitic lesions. Later investigators, on the contrary, arrived at different conclusions and decided against the employment of the Wassermann reaction on post-mortem blood because they found a very considerable number of positive reactions in cases in which not the slightest probability of the existence of syphilis was apparent. Von Bruck expressed the notable assertion that "the Wassermann reaction is a biologic, not a cadaverish phenomenon." The opinion prevailed that the positive Wassermann reaction on post-mortem blood had only a relative value because such reactions now and then appeared among non-syphilitics, although most often among patients in whom syphilis was evident.

The tests reported by Stuart Graves[3] in this paper

(3) Jour. Immunology, December, 1916.

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have been done on sera taken under aseptic precautions from 290 patients who have come to autopsy in the pathologic laboratory of the Medical Department of the University of Louisville and of the Louisville City Hospital. Tests have been made twice a week, so that serum has been kept at the longest not more than eighty-four hours and then under cold, sterile conditions. The serum has rarely stood in contact with the clot in the tube longer than forty-eight hours. The bodies have been those of patients who have died in the City Hospital and of patients who died outside the hospital and have been sent to the laboratory by the coroner for examination.

The author found that the post-mortem Wassermann reactions confirmed ante-mortem reactions in 95 per cent. of thirty-eight control cases. Positives were confirmed in serum six hours post-mortem and negatives in serum twenty-two hours post-mortem.

In 90.4 per cent. of cases showing post-mortem anatomic lesions of syphilis or presenting positive evidence of syphilis in their histories the sera post-mortem gave positive Wassermann reactions.

The fact that positive post-mortem reactions appeared in thirty-eight cases, which did not present post-mortem lesions or historic evidence of syphilis and in which death was due to acute infections—tuberculosis or malignant tumors—can not be interpreted to mean that the reaction was caused by those diseases because, in the first place, the histories and autopsies in those cases were not sufficiently complete to exclude syphilis, and in the second place, because sera from ninety-four patients who died of acute infections—tuberculosis or malignant tumors—examined under similar conditions, gave negative reactions.

Only 7 per cent. of 282 cases showed negative reactions in the presence of anatomic lesions (aneurysms) characteristic of syphilis. The reactions conformed to the anatomic and historic evidence in 84 per cent. of the cases. The fact that only eight, or 3 per cent., of the sera were anticomplementary indicates that the sera were in good condition. The average percentage of specific reactions was almost as high post-mortem as would

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be expected ante-mortem. The positive reaction appeared in twice as many males as females, in three times as many negroes as whites and in white females in only 4.3 per cent. of the cases examined.

The Wassermann reactions, performed on post-mortem blood according to the methods followed in this investigation, is a reliable aid to the diagnosis of syphilis.

Comparative Study of Different Methods of Performing the Wassermann Test. A modification of the Wassermann antigen, which has gained very enthusiastic and almost general adoption, is that involved in the addition of cholesterol to the tissue extracts formerly used. In 1910, Browning, Cruikshank and McKenzie showed that the quantity of complement absorbed by a mixture of lecithin (watery emulsion of an alcoholic solution of lecithin) and inactivated syphilitic serum could be greatly increased by the admixture of cholesterol.

There can be no question that the addition of cholesterol to the alcoholic extract renders the latter more powerful as an antigen and that considerably more positive results are thus obtained in the practical testing of human sera. The accuracy and reliability of these additional positive results, however, have been questioned. Thus Kolmer pointed out that cholesterolized alcoholic extracts may give some inhibition of hemolysis with normal sera and must, therefore, be very carefully controlled. However, he places them first in order of practical efficiency in diagnosis. Zinsser also has sounded a warning against too implicit reliance upon the cholesterolized antigen.

In a communication by J. W. Smith and W. J. MacNeal[4] are presented the results of 496 Wassermann tests upon 477 patients by three different methods, together with brief clinical notes upon those in whom the diagnosis of syphilis was doubtful. In each case the test was performed with an antigen of simple alcoholic extract at 37° C., a cholesterolized alcoholic extract at 37° C., and a simple alcoholic extract at 8° C. (ice-box temperature).

In a group of 110 syphilitic individuals in various

(4) Jour. Immunology, December, 1916.

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stages of the disease, the cholesterol-reinforced antigen with incubation at 37° C. gave 58.2 per cent., the simple antigen at 37° C., 32.2 per cent., and the simple antigen at 8° C., 77.1 per cent. of positive tests.

In a group of forty-three patients, probably syphilitic, the first method yielded 65.9 per cent., the second 1.6 per cent., and the third 5.0 per cent. of positive tests.

In a group of 265 non-syphilitic patients, tests by all methods were negative throughout.

The writers conclude from the results of their work that the use of a simple alcoholic antigen, with the first incubation carried out in the ice-box for from four to twenty-four hours, is more sensitive in the detection of syphilis than the other procedures tested. Furthermore, a positive result thus obtained is much more trustworthy evidence of syphilis than is a positive fixation with a cholesterolized antigen.

Standardization of the Wassermann Reaction. The great fault to be found with the Wassermann test, and the one for which the serologist can offer no excuse, is the false positive reaction, which occurs entirely too often and too frequently plays havoc with the lives of innocent victims. It is due either to errors in technique or to errors in judgment in reading and reporting results. The technical errors are guarded against by the controls with serum alone, with antigen alone, and with a known negative serum. Only the control with a known positive serum remains to be marshalled against the danger of drawing the reaction too fine, and this is proposed by Stillians.[5] The errors of judgment responsible for false positive reactions are more difficult to dispose of. As a means to this end, the formulation of definite rules as to what should or should not be reported as a positive reaction is desirable. This leads to the necessity of a standardization of the Wassermann reaction, long desired, but difficult to attain. So many are the slight variations in the technique even of those who perform the real Wassermann reaction, that hardly two serologists can be found who agree on the best methods throughout the test. The New York committee appointed in 1915 by Emerson to consider this subject,

(5) Amer. Jour. Syph., October, 1917.

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found it impracticable to attempt to reconcile the different methods or to prescribe a standard technique. A standard is required which is adaptable to any technique, which will show exactly when the reaction is at its point of highest efficiency, when it is too weak, allowing weak positive sera to escape detection, and when too strong, overstepping the limit of safety, beyond which lies the false positive reaction.

To obtain a standard positive control, it is necessary to have a serum preservative which will allow of the use of the same positive control over a long period of time. The method of preservative suggested by Reudiger which consists in the addition of an equal amount of glycerine has been found by Stillians to be perfectly satisfactory. As Reudiger warns, glycerinized sera tend to become anticomplementary. In the preservation of negative or weak positive sera, tested in the full dose, 0.2 c.c., this is of importance; but in the case of very strong positive sera, giving full deviation of complement with a very small amount of serum, the anticomplementary action of the glycerine is negligible. Strong positive sera thus preserved for over four months have not changed in strength. Most of them have been kept in the refrigerator, but several specimens exposed to summer temperature for over a month have shown no change. No attempt has been made to sterilize the glycerine, nor to protect the glycerinized serum from contamination beyond the observation of ordinary cleanliness. Owing to the difficulty of measuring glycerine accurately, the glycerinized serum has been titrated parallel to the fresh serum, and any variation recorded for the correction of future tests.

Titration of serum has not found favor with many serologists because of its variability, due to its sensitiveness to variations in the strength of the reaction. This sensitiveness makes it a very delicate index of such variations, affording accurate means of comparing tests made at different times or in different laboratories. A mixture of several very strong positive sera preserved with glycerine is titrated with the full dose of a certain antigen each time the Wassermann reaction is made. A few trials will show the titer of this mixture when the

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reaction is at its point of highest efficiency. The mixture of glycerinized sera can then be titrated as the positive serum control with each set of tests, showing exactly the strength of the reaction, whether stronger or weaker than it should be. If much weaker, sera giving negative reactions should be retested. If stronger, the danger of false positive reactions will be recognized. For instance, the control serum titrates, at the point of maximum efficiency, 0.01 c.c., that is, 0.01 c.c. is the smallest amount causing complete deviation of complement. If a set of tests result in a titer of 0.005 c.c. for the control, all weak positive sera are retested before being reported. If on another occasion, the titer of the control serum rises to 0.02 or 0.05 c.c., sera giving negative results in this set of tests are retested.

[We have found the glycerinized control serum to be reliable and a great convenience.—EDITORS.]

This method of standardization necessitates, of course, standardized antigens. Such a possibility was suggested long ago in the fact, brought out by Boas, that the serum of most cases of early, untreated secondary syphilis titrates with good antigens, 0.01 to 0.05 c.c. Such a standard has been maintained by Stillians for several years, and to require of all serologists that their antigens measure up to it would be no great hardship. When the serum from one guinea-pig is used as complement, considerable variation in the strength of good antigens must occasionally be expected, but they should not be rejected on this account, and this difficulty can be overcome by the use of a mixture of sera as complement.

The mixture of glycerinized positive sera may be valuable not only as an added protection to the serologist using it as his positive serum control, but might easily be used for standardization of the reaction in the various laboratories. A central depot, under government control, perhaps, could make up and standardize such a mixture of strong positive sera in large quantities, giving it out in small amounts to the various serologists to use in standardizing their own positive control mixtures. Before one such standard control

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is used up, another supply can be made and standardized by parallel titration.

Large Quantities of Blood Serum in the Wassermann. Bohan and Lynch[6] recommend the use of large amounts of serum in order to catch slightly positive reactions.

At least 10 c.c. of blood should be obtained and as much spinal fluid as can be taken with safety, from 10 to 15 c.c., if possible. After the blood is centrifuged and the clear serum inactivated, it is transferred to a small centrifuge tube to which is added 0.1 c.c. of pure, undiluted, thoroughly washed sheep corpuscles. It is then shaken and allowed to stand for one-half hour in the ice chest. The serum is again centrifuged to throw down the sheep corpuscles, and the clear serum pipetted off ready for the test. In this way natural antisheep hemolysin is removed by absorption.

A titration for the proper unit of complement is made with a 2.5 per cent. suspension of sheep corpuscles, a known titer of immune rabbit serum and a 1:10 dilution of fresh guinea-pig serum. This is done in the presence of the different amounts of serum or spinal fluid to be used in the test: in the case of blood serum, 0.1, 0.3, 0.5 and 1 c.c. The serum is taken from a known negative case. When working with spinal fluid, the titration is done for amounts as high as 10 c.c. The spinal fluid being hypotonic for sheep cells, it becomes necessary to add sufficient sodium chloride to make an isotonic solution.

The proper units of complement having been determined, the tests are set up, each serum being run in the amounts mentioned, namely, 0.1, 0.3, 0.5 and 1 c.c. Two units of complement are used for each different amount of serum, and each individual amount is controlled for anticomplementary properties. An alcoholic extract of human heart muscle, to which was added 0.2 per cent. of cholesterol, is used as antigen in this technique. Sufficient salt solution is added to each tube, so that when the test is complete there will be 4 c.c. in each, for it is for this total amount that the titration for the complement unit is made.

One and one-half hours in a water bath at 37 C. is

(6) Jour. Amer. Med. Ass'n., Oct. 13, 1917.

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allowed for the fixation of complement, after which the unit of amboceptor and the sheep cells are added, and the final readings are made at one-half hour intervals for two hours. It is to be noted that with the larger amounts of serum the end-reaction is slower in taking place, but with an active amboceptor the final reading can safely be made at the end of two hours.

Methods of Performing the "Daily Titrations" for the Wassermann Reaction. Errors in the Wassermann test are serious, and not infrequently a false positive and a false negative may be traced to a failure on the part of the operator to titrate daily the amboceptor and complement. Ottenberg[7] gives the method he considers best for carrying out this titration for the purpose of determining the proper dose of the two reagents.

The strength of guinea-pigs' complement varies greatly. There are in general two different methods employed by different workers to compensate for this varying potency in determining doses of complement and amboceptor for use in the Wassermann reaction as well as in complement-fixation with bacterial antigens. These methods are (1) keeping the dose of complement constant and varying the dose of amboceptor from day to day according to the varying strength of the complement; and (2) keeping the dose of amboceptor constant and varying the dose of complement from day to day according to its varying strength. The fact does not seem to have been recognized that these two procedures represent entirely different things and produce different results.

No author gives any reason for adopting the one or the other procedure. Followers of each method are found among those who adhere to the original requirement of a hemolytic system of two units strength, and among those who attempt to reduce the hemolytic strength to one unit above the strength necessary to neutralize the anticomplementary agents present in the tests.

Separate experiments were performed on each of two plans of determining hemolytic strength, namely, the system of using two units and the system of using

(7) Jour. Immunology, December, 1916.

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one unit as determined in the presence of antigen and normal serum. Positive sera were used in twelve graded dilutions from 1-2 up to 1-32 so that certain dilutions would correspond in reacting strength to weakly positive sera. Care was taken to select only positive sera that contained no natural hemolysin for sheep cells.

The antigen used in most of the experiments was a single alcoholic extract of beef heart, but enough experiments were done with a cholesterolized (0.4 per cent.) human heart extract to demonstrate that the type of antigen made no difference.

The complement used was generally the mixed complement of four or five guinea-pigs, but in certain experiments the sera of several individual guinea-pigs were separately titrated and one or two of those which showed a high complement titer were used separately.

The author's results demonstrate that the method used by many workers of compensating for increased hemolytic strength of the complement by using a diminished amboceptor dose inevitably leads to a negative result in certain grades of weakly positive sera. *The correct method of compensating for complements of greater than average hemolytic strength is by using a smaller dose of complement.* The method of doing daily complement titrations followed by many workers is greatly to be preferred, therefore, to the method of keeping the dose of complement fixed and doing daily amboceptor titrations; and undoubtedly the differences between these two methods are partly responsible for the different results that have been reported from different laboratories on identical sera.

Determination of the Optimal Amount of Antigen. In the practical performance of the Wassermann reaction the doses of all the ingredients have to be adjusted to each other. The original Wassermann reaction and many of its modifications follow the principle of employing a fixed dose of complement and as large a dose of antigen as possible without danger of non-specific fixation. Usually those who follow this method also determine the least amount of antigen capable of giving a positive reaction with positive serum (the antigenic

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unit). They require that the dose actually used shall be a considerable multiple of this unit and state that the more multiples of the smallest antigenic unit contained in the dose used, the better the antigen.

On the other hand, there are many authors who use an arbitrary fixed dose of antigen and adjust the complement to the dose of antigen in such a way that the complement is capable of giving complete hemolysis in the presence of the dose of antigen used. These authors all take rather large doses of the alcoholic extracts, evidently also with the idea that the larger the amount of antigen used the more likely one is to detect weakly positive sera. Since, of course, the complement is adjusted in each case to the dose of antigen used, the dose is "safe" in the sense of not giving false positive results.

Ottenberg[8] always subscribed to this opinion, namely, that the larger the dose of antigen that could be used with safety the better results might be expected, until a chance observation led him to doubt its validity. On investigation he found that when the complement was accurately adjusted to the antigen the rule given above did not hold true at all. The experiment has been repeated a great many times and invariably resulted the same way.

The results of his experiments showed that in determining the most favorable dose of antigen one should ascertain the correct amount of complement for use with each of several doses of antigen, and then determine the complement-fixing power of each dose of antigen with its appropriate complement dose by testing it with a progressively diluted positive serum. *The dose of antigen which gives fixation with the highest dilution of positive serum is the optimal dose and this is not by any means usually the largest dose tested.*

The probable explanation of this observation is that when the dose of antigen is increased beyond a certain point the amount of complement which has to be added to overcome the anticomplementary effect is too great to be fixed by certain grades of positive serum.

This method for ascertaining the dose of antigen is of course applicable only to those systems in which the

(8) Ibid.

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complement dose is adjusted to the dose of antigen. In the other systems in which the dose of complement is either fixed (0.1 c.c.), or is two hemolytic units, the rule does not apply because the ratio of complement to antigen is always greater and hence the more one can increase the antigen dose (and still remain below the point where non-specific fixations are obtained) the better the results.

A New Method for Making Wassermann Antigens from Normal Heart Tissue. The antigen value and anticomplementary and hemolytic properties of the various lipoids of beef heart have been investigated by Neymann and Gager.[9] It was found that lecithin is the only substance of the primary ether extract of dried pulverized beef heart that had any antigenic value, and that the most important substance as regards antigenic value occurs in the secondary alcohol extract and is a di-amino-monophosphatide. On this basis of solubilities a new method for making antigens is described.

Remove all the endocardium and pericardium, larger blood-vessels and fat from a normal beef heart. Grind the heart muscle very fine and spread it in a thin layer on glass plates. Dry by means of an electric fan for twenty-four hours, turning the layer of tissue after twelve hours. A parchment-like dry sheet of tissue results. Break this up and grind again, thus producing a fine dry powder. Put this in bags and dry in an incubator at 37° C. for several days. Extract with ether in a Sohxlet apparatus for twelve hours or in an ordinary wide mouthed bottle at room temperature five or six times until the supernatant ether is no longer colored yellow. The latter procedure takes from eight to ten days. The ether should cover the muscle powder to a depth of from 2 to 3 inches. Dry the powder by spreading it out on a sheet of paper for several hours. Now extract the powder with absolute or 95 per cent. alcohol for ten days. The alcohol should cover the powder to a depth of half an inch and it will gradually assume a light yellow color. Titrate the antigen thus obtained. Extract the powder a second time with alcohol for fourteen days. Titrate this antigen.

(9) Jour. Immunology, October, 1917.

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Both extracts will prove to be good plain extracts; sometimes the second will be better than the first for the di-amino-monophosphatides seem to go into solution after groups B′ and C′ have been dissolved out.

In order to produce an acetone-insoluble extract the plain extracts are united, evaporated to dryness at room temperature by means of a fan, and treated with an excess of ether. The ether soluble portion is filtered off, allowed to evaporate, treated with an excess of acetone and the sticky brown residue is finally dissolved in a minimum quantity of absolute alcohol. The solution is then filtered and again titrated.

This preparation consists almost entirely of group E′ and with ten hearts prepared in succession has each time given an antigen which bound at least 1 to 1,600 and showed a low anticomplementary titer and no hemolytic properties.

A cholesterolized antigen can be made by adding 0.2 gram of cholesterol to 100 c.c. of the plain extract or of the acetone insoluble preparation. The cholesterol will dissolve very readily in either of these phosphatide solutions, much more readily than in the same amount of absolute alcohol. After the addition of cholesterol the antigen is again titrated.

These antigens have been in use for the past six months. They have proved reliable in every way and have solved the problem of finding a certain and definite method of obtaining a reliable, fairly equal, and powerful product. Though these antigens pick up weaker positives than former preparations, they have never given false positives.

Surface-Tension and the Wassermann Reaction. The fact that surface tension plays an important rôle in adsorption phenomena led Major Nesfield[1] to test the bearing of surface tension (S. T.) on the Wassermann reaction.

This inquiry naturally led on to a further one into the tension-lowering effect of alcohol, which is the main constituent of the antigens used in the test. The conclusions to which he came were as follows:

(1) Lancet, Jan. 6, 1917.

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1. S. T. is the all-important factor in the Wassermann reaction.

2. Alcohol, bile, phenol, and solutions of cholesterol, which act as antigens in the Wassermann test, all have very low S. T. and greatly reduce the S. T. of serum.

3. It is difficult to distinguish a syphilitic antigen from a substance which lowers S. T.

These facts are capable of easy verification, but their explanation is a more difficult matter. The question suggests itself: Did Wassermann recognize the S. T. lowering action of alcohol? He must have known but intentionally suppressed the knowledge because, the test being founded on the Bordet-Gengou reaction, few would have given credence to it if alcohol alone, or with the addition of 0.5 per cent. phenol, had been used in place of a specific extract.

In this connection the history of the test is informing. An extract of syphilitic liver was first used by extracting one gramme of liver with phenolated saline. Then it was shown that normal liver was as efficient. In each of these cases the best fluid contained bile salts and phenol. Having found that these watery extracts were unstable, alcohol was added, and it was then discovered that almost any organ of any animal produced an excellent antigen, the reason obviously being that it is the alcohol itself which is the antigen.

For the purpose of the experiments, Nesfield followed Fleming's modification of the Wassermann test, previously sensitizing the sheep's red blood corpuscles with hemolytic serum. The antigen used as a control was an alcoholic extract of human heart 2 parts, and 1 per cent. alcoholic solution of cholesterol 1 part. The procedure was as follows:

One volume of unheated serum was mixed with 4 volumes of a 1 in 20 dilution of antigen in saline. This was kept at 98° F. for 30 minutes, and then 1 volume of a 1 in 5 emulsion of the sensitized sheep's corpuscles was added and the tubes incubated again for one hour; 1 in 40 and 1 in 80 dilution of antigen were also used in each case so as to determine the degree of reaction. He put up precisely similar tubes, using 95 per cent. alcohol in dilutions of 1 in 20, 1 in 40, and 1 in 80 in

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place of the extract, and also 95 per cent. alcohol in the above dilutions, plus 1 volume 0.5 per cent. phenol.

The serum used was from patients with typical syphilis, and the controls were known to be free from syphilis. The experiments were repeated again and again, always with the same result, and lead to the conclusion that 1 in 20 alcohol absorbs alexin from syphilitic serum and not from normal. 1 in 80 alcohol, plus 1 in 1,000 phenol, acts in the same way, so that phenol, like cholesterol, increases the antigen power of alcohol, at the same time reducing the S. T.

Wassermann Paradoxus. A weakly positive Wassermann reaction is of value only when the serum comes from a patient who has been treated for syphilis. In the absence of definite signs of lues in the history or in the physical examination, or in the presence of puzzling and undefinable phenomena, a weakly positive result is of no value whatsoever. Not only are there positive reactions in non-luetic diseases, but also weakly positive reactions in people who complain of nothing and never had lues in any of its forms.

In using two antigens Kaplan[2] has found that the cholesterolized extract is usually the one giving a more complete inhibition than the crude alcoholic non-reinforced product. It is by no means a rare occurrence to have complete hemolysis with the latter and equally strong inhibition with the former.

A four plus result on a serum showing complete inhibition with both extracts becomes gradually less positive in the tubes containing the non-cholesterolized antigen as a result of proper therapy. Only after more thorough and continuous treatment does the cholesterolized tube begin to show evidences of weakening.

In reviewing his serologic material at the Neurological Institute for the past three years, Kaplan found that certain patients presented a serologic behavior just the reverse of the one pictured above, *i. e.*, their inhibition from the start was strongest, in fact repeatedly four plus in the non-cholesterolized tubes and either weakly plus or entirely minus in the reinforced test.

Upon a closer analysis from the clinical point of view,

(2) New York Med. Jour., March 10, 1917.

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a very interesting situation disclosed itself. This paradox Wassermann invariably came from patients who displayed one or more manifestations of motor unrest, such as spasms, tics, tetanoid movements, fainting spells, and convulsions. Many presented that type of epilepsy that still parades under the designation of "idiopathic." None showed signs of lues in the physical analysis or in the history. A few patients were given the benefit of the doubt, but neither mercury nor salvarsan nor the combined treatment showed any improvement in these cases. The spinal fluids when analyzed never showed an abnormal condition.

The connection between this motor unrest or spasmophile tendency and the positive results with noncholesterolized and negative with reinforced antigen is unexplainable, at least for the present. It must be borne in mind that not all cases showed this peculiarity and that many apparently similar cases resulted in a negative with both extracts.

Effect of Salvarsan on the Wassermann Reaction. In an attempt to test the fluctuation of the degree of positiveness of the Wassermann in cases under treatment and to determine if there exist such a phenomenon as the "provocative" injection of salvarsan, J. T. King[3] carefully titrated the serum of sixteen patients before and after twenty injections of salvarsan. In all, the reaction was positive before injection, but in only one was there an increase in titer. King believes it improbable that over short periods of time there occur any marked spontaneous fluctuation in the amount of complement-fixing substance in the blood of syphilitics, and that definite proof of the existence of the provocative Wassermann reaction following salvarsan is not at hand at the present time.

[We have repeatedly seen late, superficial syphilitic, cutaneous and mucous membrane lesions in patients who had been going from one physician to another in search of relief and failing in their search because the Wassermann was negative. The lesion being typical clinically, we have given them intravenous injection of small doses which served the double purpose of healing

(3) Jour. Amer. Med. Ass'n., Dec. 2, 1916.

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the lesion and rendering the Wassermann positive. This fact alone justifies the retention of the term "provocative" injection. Titration of 1,600 cases instead of sixteen would, without doubt, convince the writer of the existence of such a phenomenon.—EDITORS.]

The Provocative Wassermann Test. From a study of 103 cases in which an injection of salvarsan was given to provoke a positive Wassermann after a negative test, presumptive, but not conclusive evidence of the existence of a provocative effect was obtained by Stokes and O'Leary.[4]

It seems probable that both individual technical variations, and variations in the reagents are factors in the results in addition to the provocative effect. Positive provocative effects were obtained in 18.4 per cent. of 103 cases. It was of value in recognizing as insufficiently treated, two out of six cases (33.3 per cent.) in which it was applied to determine whether or not a cure had been obtained.

The provocative test in this series seemed to be of the least service in active deep seated visceral, osseous and central nervous system syphilis, where it was most needed, fairly efficient (40 per cent.) in latent syphilis, and most often positive in late cutaneous and mucous membrane manifestations, where the diagnosis can often be made morphologically.

The percentage of patients whose syphilis was suspected from clinical examination ran parallel to the percentage shown to be syphilitic by therapeutic test, and far in advance of the number shown to be syphilitic by the provocative test. The therapeutic test, properly applied in suitable cases, therefore appears to be of more value in clinical diagnosis of obscure syphilis than the provocative Wassermann test. Positive therapeutic effects were obtained in 63.1 per cent. of thirty-eight patients, and in 65.2 per cent. of twenty-three patients in whom the provocative test had failed to establish the presence of syphilis.

The provocative Wassermann seems to be of little value in the absence of clinical evidence of the dis-

(4) Amer. Jour. Syph., January, 1917.

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ease, and to be inferior both to clinical judgment and the therapeutic test in the recognition of obscure cases.

The Hecht-Gradwohl Test. In order to avoid the destruction of any thermolobile component of the so-called antibody in the process of heating the serum at 56° C. for thirty minutes, Hecht and Weinberg devised a method whereby the unheated serum is used.

Gradwohl[5] has modified their method and now describes a test to which he has given the name "Hecht-Gradwohl." The technique is carried out as follows:

Place in a rack fourteen small test tubes. The first ten of these tubes are used to determine the hemolytic index of the suspected blood. By this is meant the exact amount of hemolytic amboceptor present in the given blood serum. The last four tubes are used in the actual test. Add 0.1 c.c. of fresh unheated patient's blood serum to each of the first ten tubes. Then add decreasing amounts of normal salt solution to these tubes, beginning with 1 c.c., then 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, and 0.1 c.c. to the succeeding nine tubes. Next add increasing amounts of fresh 5 per cent. suspension of sheep's blood, starting with 0.1 c.c. and ending with 1 c.c. Place the rack in the water bath for one-half hour. The tube which last shows complete hemolysis constitutes the "hemolytic index;" if it be Tube 4, the index is 4, because this tube had received 0.4 c.c. of sheep corpuscles and therefore we have obtained an idea as to how much sheep blood is to be added to the last four tubes. The first three tubes (11, 12 and 13) constitute the tubes for the actual test, while the last tube in the rack (14) serves as the serum control tube. Tubes 11, 12 and 13 receive, therefore, the patient's serum, the proper amount of sheep's corpuscles, dependent on hemolytic index, rising strengths of antigen, but no complement and no amboceptor. Tube 14 receives only sheep corpuscles, but no antigen.

Gradwohl uses 0.1 c.c. of diluted antigen, determined by titration, in Tube 11, 0.15 c.c. antigen in Tube 12, and 0.2 c.c. in Tube 13. In order to equalize the volume of fluid in all these tubes, add 0.2 c.c. normal saline to Tube 11, 0.15 c.c. to Tube 12, 0.1 c.c. to Tube 13, and

(5) Amer. Jour. Syph., April, 1917.

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0.3 c.c. to Tube 14. The tubes are then agitated and placed in the water bath for half an hour. These last four tubes are filled at the time the additions to the first ten are made and are left with them in the water bath for one-half hour for fixation of complement, after which the rack is taken out and the hemolytic index computed. If the index be low, say from 1.4, add 0.1 c.c. of sheep's blood to the last four tubes. If the index be between 5 and 7, use 0.15 c.c. sheep's blood to the last four tubes; if between 8 and 10, add 0.2 c.c.; if the index be over 10, rack up ten more tubes and repeat the titration of the natural complement and amboceptor, then estimate that; if between 11 and 15, use 0.25 c.c.; if between 15 and 18, use 0.3 c.c.; and if between 18 and 20, use 0.35 c.c. If the patient's serum has an index below 2, regard the reaction as of doubtful value. If it be above 2, regard it as absolute. The reaction is read off exactly as in the Wassermann, that is, inhibition or noninhibition of hemolysis. If the amount of complement or natural antisheep amboceptor is very low, add the proper amount of guinea-pig's serum or rabbit's immune serum, ascertained by preliminary titration.

[The difficulties we have encountered in the use of this method are the low hemolytic titer of many of the sera, and the number of false positives which the method, or at least our use of the method, has given. The first difficulty may perhaps be overcome by the modification of Bartlett and O'Shansky (*vide infra*) and the second by the proper selection of the antigen (*vide* Kolmer *infra*).—EDITORS.]

The Hecht (Gradwohl Modification) Complement-Fixation Reaction. A careful study of the comparative results of the Wassermann and the Hecht-Weinberg reaction as modified by Gradwohl has been made by Kolmer.[6] He used four different types of antigens and all reagents were well titrated and the reactions carefully controlled. He found that the reaction constitutes a very delicate control over the Wassermann reaction.

About 92 per cent. of sera consisting mostly of those

(6) Jour. Immunology, December, 1916.

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collected within a period of forty-eight hours at the time of the tests, were found to contain sufficient complement and natural anti-sheep hemolysin for the conduct of the modified Hecht reaction. In those sera deficient in one or both of these substances guinea-pig complement or immune hemolysin must be used, but the addition of these alters the nature, sensitiveness and value of the reaction.

The modified Hecht reaction possesses a greater negative than a positive value, because it is open to the error of falsely positive or proteotropic reactions, as obtained in the Noguchi test employing active or unheated serum.

The Hecht reaction yielded about 4 per cent. of falsely positive reactions or pseudo-reactions with one or more of the three different antigens used in this study; the fewest of these pseudo-reactions occurred with an extract of acetone-insoluble lipoids.

The antigen or antigens employed in the modified Hecht reaction must be carefully standardized at frequent intervals in order to reduce the percentage of pseudo-reactions to a minimum.

A suitable extract of acetone-insoluble lipoids of heart muscle generally proved the superior antigen for the Hecht-Gradwohl reaction. An alcoholic extract of syphilitic liver proved of least antigenic sensitiveness and yielded the highest percentage of false reactions or pseudo-reactions.

The modified Hecht and Wassermann reactions, including the use of cholesterolized extracts, yielded similar results in 82 per cent. of a series of 360 sera.

The modified Hecht reaction yielded about 16 per cent. more positive reactions and about 12 per cent. more *true* positive reactions than the Wassermann reaction conducted with a cholesterolized extract as antigen; 26 per cent. more *true* positive reactions than the Wassermann conducted with an alcoholic extract of liver and 18 per cent. more *true* reactions than the Wassermann with an extract of acetone-insoluble lipoids.

The modified Hecht reaction has its greatest value as a serologic control in the treatment of syphilis. During treatment, the Wassermann reaction with an alcoholic extract of syphilitic liver is usually extinguished

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first and after considerably more treatment it is generally extinguished in the reaction with a cholesterolized extract; the Hecht reaction is usually last to react in a negative manner.

Suitable and standardized cholesterolized alcoholic extracts of heart muscle constitute the most sensitive antigens in the Wassermann reaction with which we are familiar and with experience Kolmer's confidence in their reliability has steadily increased. In the author's opinion it is a serious error to regard a person as cured of syphilis on the basis of a negative Wassermann reaction conducted with an alcoholic extract of syphilitic liver alone.

A Modified Gradwohl Wassermann Technique. After employing the Gradwohl method in a series of cases, a further modification was made by Bartlett and O'Shansky,[7] by which it became evident that the natural complement of human blood serum combines with great readiness with the syphilitic antibody in the presence of lipoidal antigens. This union occurs much more readily than does that between the same complement and the anti-sheep amboceptor of the patient's serum in the presence of sheep corpuscles. In fact, this is so marked that if the proper quantity of the patient's serum be employed, the sheep corpuscles may be added to the tubes at the same time as the lipoidal antigen is added and then incubated without any previous period of complement-fixation. The results are so constant that it appears that this technique may be employed to advantage to control the routine Wassermann test. As the patient's serum in this method is necessarily used without inactivating, there is no decrease of the syphilitic antibody as probably occurs in heating serum to 55° C. for 30 minutes; also as the serum is not incubated at 37° C. before the sheep corpuscles are added, there is no destruction of complement and only a minimum amount of serum need be used for the test. The authors have now employed this method in a series of 900 cases, paralleled by the routine Wassermann test, with satisfactory results.

They have tried the method of Gradwohl in 250 cases

(7) Amer. Jour. Syph., October, 1917.

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controlled by the routine Wassermann test and also paralleled by their method and it has not proved entirely satisfactory. In 14 per cent. of the cases no hemolytic index could be obtained. In about 64 per cent., when an index was obtained, it was so low that, according to Gradwohl's own statement, the results of the reaction must be regarded as of doubtful value. In this 64 per cent., and in the remaining 22 per cent. when the index was higher, the results did not agree well enough with those of the routine Wassermann test to make the method appear to be of great value. Nor did it prove more sensitive than the regular Wassermann test. On the contrary, it gave a smaller number of positive tests. This appears to be due to the discrepancy between the amount of sheep corpuscles used for the test and the entire amount which the same quantity of serum used can hemolyze as shown in the hemolytic index; in other words, this is due to the use of an excessive quantity of either complement or amboceptor, or both. However, it is only fair to state that the only antigen used in making these tests by the Gradwohl method was an alcoholic extract of human heart, half saturated with cholesterol.

The technique of the Gradwohl test for determining the hemolytic index was then modified by using a definite quantity of sheep corpuscle suspension in each tube and finding the smallest amount of the patient's serum which would produce complete hemolysis in 30 minutes in the water-bath at 37° C. The amount of sheep corpuscles determined upon was the same as that employed in the routine Wassermann test, namely, 1 c.c. of a 5 per cent. suspension in each tube, the entire quantity of material in the tube eventually being made up to .5 c.c. The technique is shown in the accompanying table.

FINDING THE HEMOLYTIC INDEX IN THE MODIFIED METHOD DESCRIBED.

Tubes	1	2	3	4	5	6	7	8	9	10
Unheated serum	.01	.02	.03	.04	.05	.06	.07	.08	.09	.10

.5 per cent. sheep corpuscles—.1 c.c. in each tube.
.85 per cent. salt solution—Up to .5 c.c.

Incubate in the water-bath for 30 minutes at 37° C. Shake occasionally. Read index.

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The tube containing the smallest amount of serum which shows complete hemolysis is taken as indicating the hemolytic index.

Especial care must be exercised in determining the hemolytic index to make sure that the reading is sufficiently high. That is, if there be the least suspicion of any turbidity remaining in a tube when it is compared with one undoubtedly showing complete hemolysis, the next higher in the series must be taken as showing the index.

In comparing the results of the modified test described and the routine Wassermann test, the authors obtained in the 900 sera sixty-four which gave no hemolytic index. Of the remaining 836, there were 629 which were negative by both tests, while 166 were positive by both tests. Thus, 795 agreed by both tests. Ten sera were positive with the routine Wassermann test and negative with the modified test described. Twenty-nine were positive with the modified test described and negative with the routine Wassermann test.

The method has been found to be more delicate than the routine Wassermann test and, according to the results so far obtained, is more reliable. It is not advocated as a method to replace the routine Wassermann test, but one to be given a trial paralleled with that test until its value be determined.

Luetin Test in Non-syphilitics. The luetin test has now been shown to be untrustworthy by many different, and independent workers. H. N. Cole and H. V. Paryzek[8] found that out of thirty-nine cases tested by the luetin reaction, two normal persons gave pustular reactions to the control test. Among eighteen patients taking potassium iodide, sixteen gave positive reactions: the reactions were most strongly positive in those patients who had received from 200 to 600 grains.

This reaction is found not to be specific for potassium iodide alone, as it was caused, though in a lesser degree, by sodium bromide in three cases, by potassium nitrate in six out of eight cases tested, and by calcium bromide and by sodium iodide each in one case tested.

(8) Jour. Amer. Med. Ass'n., April 14, 1917.

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A "Luetin" Reaction in Syphilis Produced by Agar. The non-specific character of the luetin test was well demonstrated by J. H. Stokes,[9] inasmuch as he was able to produce clinically similar lesions by injections of agar in normal saline.

The agar reaction differs from the luetin reaction chiefly in a tendency to a more torpid course and a slower development. Papular and pustular reactions may be produced, the latter being somewhat more hemorrhagic than those produced by luetin. The percentage of positives in known syphilitics, eliminating doubtful reactions, varied in two series aggregating forty cases, from 50 to 70 per cent.

The normal persons and non-syphilitics in the series did not react. The only positive case in which syphilis seemed to be eliminated was a case of urticaria pigmentosa with factitial urticarial phenomena. Two patients with gonorrhea in a total series of seventy-six reacted positively. Both were receiving vaccines with marked reactions. One patient with sycosis barbae, receiving vaccines with marked reactions, also reacted positively to the agar.

The influence of iodides could be eliminated from the series in which 50 per cent. reacted positively.

The positive reaction to agar as brought about by the internal administration of iodides was observed in typical form in three cases. It is simply a severe form of the luetin and agar reactions. In two cases in which iodides were being administered, the reaction to agar was negative.

The cutaneous reaction to both luetin and agar in syphilis is interpreted as non-specific in character and as a colloidal absorption phenomenon in a hypersensitive or labile skin.

[The accumulation of evidence showing the non-specificity of the luetin reaction appears to be sufficiently weighty to discredit a test which at first seemed to be a valuable contribution to medicine.—EDITORS.]

Indigo Test for Syphilis. In the issue of the *Münchener medizinische Wochenschrift* for Sept. 7, 1915, von Dungern described a test for the serum diagnosis

(9) Jour. Amer. Med. Ass'n., April 14, 1917.

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of syphilis with chemical reagents. Although an adequate theoretical basis for this phenomenon had not as yet been secured, von Dungern believed that it was practically applicable to the diagnosis of syphilis.

The test was founded upon the observation of Karl Jaudas, von Dungern's assistant, that the heat coagulation of normal serum is prevented by a smaller relative quantity of an alkaline solution of indigo than is the case with the sera of syphilitics.

E. P. Flood[1] has investigated the reaction and finds that neither the indigo nor the salt content of the reagent takes part in the inhibition of the coagulation. The alkali is the sole inhibiting agent.

von Dungern further stated that with similar amounts of the reagent this inhibition was less marked in syphilitic than in normal sera. In Flood's experience such a difference was present in but very slight degree and with no constancy.

The method is of no value in the serum diagnosis of syphilis, for in the entire series of 140 sera, forty of which were evidently syphilitic, coagulation occurred in but three, with the prescribed amount of reagent.

Spirochetal Content of the Spinal Fluid. The question as to the spirochetal content of the spinal fluid is a matter of very great importance not only for the bearing that their presence may have upon the pathology of the disease, but also from another standpoint. The spinal puncture has today become a routine measure in all well-regulated hospitals and is performed, or should be at least, at some time during every syphilitic's lifetime. It not infrequently happens in withdrawing the stilette or in collecting the fluid that more or less is spilled over the operator's or attendant's fingers, and in the laboratory the possibility of the fluid being a source of infection is customarily entirely disregarded. If spirochetes be present in spinal fluid the same great care should be used in examination as is employed in the examination of other syphilitic products and secreta.

At the University Hospital clinic at Ann Arbor, specimens of spinal fluid are withdrawn from every patient having syphilis upon entrance into the hospital

(1) Jour. Immunology, December, 1916.

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as a routine diagnostic measure. Many unsuspected cerebrospinal involvements have been uncovered by this routine procedure.

During the past year Wile[2] has inoculated the spinal fluid from eight cases of acute cerebrospinal syphilis, general paresis, and tabes dorsalis into the rabbit testis. The results confirm the original observations of Uhlenhuth and Mulzer, Nichols and Hough, and others, that the spinal fluid contains spirochetes and that as such it is an infectious fluid. Injections of the cerebrospinal fluid from two cases of acute cerebrospinal syphilis resulted in positive takes in both. Injections of the spinal fluid from three cases of general paresis resulted in positive findings in two. Injections of the spinal fluid from three cases of tabes dorsalis resulted in a positive result in one and negative in two.

These results contain some interesting data. In the first place, in not a single case was a permanent experimental syphilis in the sense of definite testicular nodules, elicited. In all the cases in which the spirochetes were positively found, these remained in the testis and then gradually disappeared. The interpretation of this finding is somewhat difficult. It may very well be that the organisms in the spinal fluid were in too small a quantity or too attenuated in virulence to produce permanent lesions in the rabbit. The second possibility which suggests itself is that notwithstanding the failure to find the organisms in the fluid before the injections, that these were present and that they persisted in the rabbit testis as survivals. In this case their disappearance might be explained upon their transplantation to a new soil. Inasmuch as the rabbit testis had shown itself an ideal soil for spirochetal culture, the latter explanation would hardly seem to suffice.

It would seem that the absence of a distinct nodule in the rabbit testis must not be regarded as proof of a non-take. Swelling of the organ without definite nodule formation occurred in three cases, and in all these cases, organisms were found for a variable length of time. The possibility that the spirochete may exist in the spinal fluid as a resting stage has been suggested,

(2) Amer. Jour. Syph., January, 1917.

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although Zinsser, Hopkins and Gilbert, as well as Uhlenhuth and Mulzer, doubt the existence of any ultramicroscopic forms.

Whether or not such resting stages, ultramicroscopic or not, exist, the presence of spirochetes in the spinal fluid must be accepted in the light of our present knowledge that they exist in the nerve tissue itself which is bathed by the fluid.

There appears to be no recorded case of accidental syphilitic infection from contact with cerebrospinal fluid. Such an accident, however remote, must be regarded as possible in the light of this and previous investigation. In the University Hospital clinic at the present time the same care is exercised in handling spinal fluid as in the handling of any of the more infectious syphilitic secreta.

A further point of some interest lies in the fact that those cases were positive in which there was a high pleocytosis. This suggests at least that the organism may be in some way connected with the lymphocytes. That this is not invariably the case, however, is illustrated by the case before mentioned of Uhlenhuth and Mulzer, in which the lymphocytosis was not great. The spinal fluid in any case of cerebrospinal syphilis of whatever form, probably contains spirochetes at certain times during the course of the disease. The negative inoculation results mean nothing. The quantity of fluid used may have been too small, the organisms in an attenuated condition, or physical conditions in the one medium so different from those in the other that they did not flourish. The high percentage of positives, 62.5 per cent., is a far more significant finding.

TREATMENT.

Salvarsan and Neosalvarsan in Syphilis. After an experience of more than six years with salvarsan and neosalvarsan, Oliver S. Ormsby[3] states that salvarsan and neosalvarsan are the most efficient drugs yet discovered in the treatment of syphilis. Alone they have completely eradicated the infection in early cases before the Was-

(3) Jour. Amer. Med. Ass'n., March 31, 1917.

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sermann reaction has become positive. The large number of reinfections testify to this fact. Yet even in these cases mercury is recommended as an adjunct.

In all other cases, mercury should always be an accompaniment of salvarsan, and in many cases potassium iodide is indicated, especially in the so-called tertiary and latent cases and in those involving the nervous system. The ability of potassium iodide to remove infiltrations, gummas and nodules, together with its marked effect on vascular implications, renders its use imperative.

The greater number of reactions following the use of salvarsan and neosalvarsan are insignificant. The more serious ones are to be avoided, so far as possible, by an initial small dose to test the tolerance of the patient, by careful attention to details in administrative technique, by recognizing contraindications and, in the case of early, active syphilis, preceding the salvarsan treatment with mercury, to prevent neuro-recurrence; and, finally, by giving sufficient treatment to control the disease. Emphasis must be laid on the latter statement, as much harm may be done by its apparent effect, the degree of relief giving the patient a feeling of false security; therefore, sufficient treatment is demanded to prevent recurrences and relapses.

Many of the earlier cases, following insufficient treatment, of rapid onset of symptoms which ordinarily come late in the disease, such as nervous involvement and precocious tertiary manifestations, were eradicated by more salvarsan, and now should be entirely avoided by treatment of sufficient intensity and amount to control the disorder.

The treatment of syphilis with salvarsan and neosalvarsan has caused an intensive study over the entire world of the question of efficient management of the disease, to such a degree that great lessons have been learned and much good accomplished. Their ultimate value will require many more years to determine.

As to a choice between the two drugs, salvarsan and neosalvarsan, the extensive use of both proclaims their efficiency, so that individual circumstances with the physician and patient must decide which, under the cir-

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cumstances, is to be selected. The apparent preponderance of opinion that salvarsan is more efficient is offset to a degree by the difficulties of its administration and the more frequent reactions following its use. The problem of reducing toxicity to a minimum rests with the producers of the drug.

Concerning the dangers following the individual injections, many warnings have been given to exercise care after the fourth injection. The warning has not been accompanied by tabulated results showing proof of this contention. On the other hand, the statistics now available show that the greater number of severe reactions, untoward results and fatalities have followed the first injection, and that with subsequent injections these results have greatly decreased.

[Under the "Trading with the Enemy Act" further importation of salvarsan and neosalvarsan will be impossible during the present war. License has been granted to three laboratories in the United States for the manufacture of these preparations. The best known of these, and a product that is safe and efficient, is arsenobenzol, prepared by the Polyclinic Laboratories of Philadelphia (*vide.* Practical Medicine Series, Vol. IX, 1916, p. 222). —EDITORS.]

Toxicity of Arsenobenzol (Salvarsan). Within the past five years an enormous number of publications have appeared bearing upon the clinical results of the administration of dioxydiamino-arsenobenzol dichlorhydrate, marketed by the Farbwerke Hoechst Company of Frankfort, Germany, under the name of salvarsan. The accumulated experience on this subject has definitely established the fact that this drug is the most remarkable synthetic chemical compound introduced into medicine, and is the premier remedy in syphilis, yaws (frambesia), relapsing fever, and in certain other affections. Millions of doses of salvarsan and of essentially identical compounds marketed under various names, have been administered. A number of accidents and fatalities have resulted, which although small in proportion to the vast number of doses given, constitute in the aggregate a sufficiently imposing number to warrant greater attention and study of the toxicity of

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dioxydiamino-arsenobenzol, and of the factors bearing upon it, than have been devoted to it in the past.

The present studies by Schamberg, Kolmer and Raiziss[4] were undertaken with the view of shedding some additional light upon the complex and important subject of the toxicity of salvarsan. The authors first considered the influence of certain factors related to the technique of administration of the drug, and their bearing upon toxicity.

It was found that salvarsan may be used in concentrated solutions up to 0.6 gms. in 10 c.c. in *animals*, without any evident increase of toxicity. The failure to neutralize solutions of salvarsan with alkali leads to an increase in toxicity of from 50 to 60 per cent. in solution of 0.5 to 1 per cent. concentration. The addition of a moderate excess of alkali beyond the amount required for neutralization does not increase the toxicity, as determinable by the duration of life of the experimental animal. It is possible, however, that it may have other untoward effects. The use of sterile, fresh distilled water appears to possess advantages over sterile, stale distilled, or non-distilled water as regards toxicity, although the difference in the experiments was not pronounced.

Salvarsan in alkaline solution tends to undergo oxidation on standing, with consequent increased toxicity, but this substance and its congeners vary considerably in the rapidity of oxidation and in the degree of associated toxicity. The drug should be used reasonably promptly after preparation. If two or three hours' delay be unavoidable, the solution should be kept in a cylinder, full to the stopper, so that no air be present.

Several different types of reactive symptoms may occur after the use of salvarsan; (*a*) immediate; (*b*) early and (*c*) delayed. The immediate symptoms are due to a paresis of the blood-vessels; the early symptoms coming on a few hours after the injections are febrile and gastrointestinal, and the delayed symptoms may be referable to the brain or the liver and gastrointestinal tract. There is no one cause of reaction. The etiologic factors in the production of reactive phe-

(4) Jour. Cut. Dis., June, 1917.

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nomena may be related to (*a*) the patient, (*b*) the technique, and (*c*) the medicament. They believe that the most important factor in the causation of reactions is referable to the drug and also that the immediate vasoparetic reactive symptoms are due to traces of an unidentified impurity in the drug, which they have for convenience termed *substance X*. It is fairly certain that these symptoms are not due to "arsenoxide." Inasmuch as salvarsan and its congeners are not compounds of absolute chemical purity, one can not, therefore, expect absolute constancy in biologic effects. The drug may vary, within certain limits, in therapeutic effect, and to a greater degree in toxicity. The ampoules obtainable in the open market exhibit striking variations in toxicity. Even the most toxic compounds, however, are tolerated by animals in much higher amounts than the maximum dose administered to man, so that there is nearly always a latitude of safety.

The authors believe that the commercial products should be tested out intravenously as well as subcutaneously, and that they should be tolerated by rabbits in the dose of 60 mg. per kilo of body weight.

Salvarsan is a safer substance than mercury and can be tolerated intravenously by white rats in fifty times the dose of the latter, weight for weight.

Administration of Arsenobenzol by Mouth. A paper by Schamberg, Kolmer and Raiziss[5] presents studies undertaken to shed additional light on the possibility of employing the gastro-intestinal tract as an avenue of administration of salvarsan. In these studies their own product, arsenobenzol, was employed.

The first object of the investigations was to determine the effect of salvarsan administered by mouth on the parasites in the blood of animals infected with experimental trypanosomiasis. These parasites react chemotherapeutically in a similar manner to that of *Spirochaeta pallida* and offer, therefore, a most excellent therapeutic criterion of the effect of various agents.

Trypanosoma equiperdum, the organism which produces dourine, or horse syphilis, was the parasite chosen. The drug was administered to rats and rabbits in solu-

(5) Jour. Amer. Med. Ass'n., Dec. 23, 1916.

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tion by means of a stomach tube, and also in the form of pills and in capsules.

Their experiments on animals demonstrated that arsenobenzol (salvarsan) can be administered by mouth in solution or in capsules and become absorbed into the blood. The proof that absorption takes place is evidenced by the fact that a distinct destructive influence on trypanosomes in the blood of experimentally infected animals is exerted. In a general way it may be stated that about one-ninth or one-tenth of the dose required in solution by mouth produces an equivalent effect intravenously. In capsules it exerts, however, from 40 to 50 per cent. of the trypanocidal effect produced by neosalvarsan intravenously. It was found that the drug can be administered in capsule form over long periods of time without harmful results.

Clinically it was found possible to give the drug in doses of 30 mg. (1/2 grain) three times a day for many weeks without producing disturbing symptoms except mild digestive distress, and this is only in a relatively small proportion of cases. Administered in this way, arsenobenzol (salvarsan) is capable of producing a curative influence on the lesions of syphilis. The effect, however, is much less vigorous than when the drug is administered intravenously. The authors do not advise the use of arsenobenzol (salvarsan) by mouth as a routine. Its use is to be reserved for patients who for some reason can not take the drug by intravenous infusion or intramuscular injection.

Subconjunctival Injections of Salvarsanized Serum in Management of Ocular Syphilis. Salvarsanized serum prepared according to the method of Swift and Ellis has been found by Lamb[6] to be of great value when injected beneath the conjunctiva in iritis, iridocyclitis, kerato-iritis and interstitial keratitis. Serum derived from the blood of patients who had been given injections of preparation allied to salvarsan was found to give good results, but showed greater irritative reactions and slower resolution of the chemotic conjunctivae.

[We have found arsenobenzol prepared by Shamberg

(6) Amer. Jour. Syph., January, 1917.

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to be no more irritating when injected intraspinally than neosalvarsan; and in some cases it has been found to be much more readily tolerated.—EDITORS.]

Intraspinal Injections of Salvarsanized Serum. In an article entitled "The Truth About Intraspinal Injections in the Treatment of Syphilis" Bernard Sachs[7] completely disposed of this method of treatment as having no value whatsoever.

Fordyce,[8] however, does not allow the statements made in that paper to go unchallenged. From his extensive experience, which is probably as great or greater than that of any other worker in this country, he insists that it is the only procedure that can be employed after the intravenous treatment fails, or when the patient develops an intolerance to arsenic and that with proper technique and experience, it is less dangerous than intensive intravenous treatment.

In tabes, certain types of cerebrospinal syphilis like meningitis, meningo-myelitis, meningo-encephalitis and in optic atrophy with positive findings in the fluid, intraspinal treatment succeeds in relieving or curing the conditions after failure of intravenous and other treatment.

In paresis with sigmata of degeneration, the most to be hoped for its temporary arrest of the encephalitis. There are borderline cases of meningo-encephalitis which simulate paresis and which are curable by the treatment in question.

The criticism of the method is based largely on the results following imperfect technique and by its employment in cases without clear indications afforded by spinal fluid examination. Aside from these reasons, it has been condemned after short and imperfect trials. In some cases the existing lesions are activated by early injections and cured by persistence in the intraspinal treatment.

Sachs' statement, says Fordyce, that it is regrettable that changes in biologic findings should be made the criterion of the efficiency of any therapeutic method is unfortunate from the standpoint of the patient as well

(8) Jour. Amer. Med. Ass'n., Nov. 3, 1917.
(7) Ibid., Sept. 1, 1917.

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as the investigator. With the exceptions noted in the body of the article, there is an intimate relationship between the clinical symptoms and the fluid findings. It is not difficult to select individual cases in which the Wassermann and globulin reactions are unchanged after prolonged treatment; but conclusions based on such exceptional cases are one sided, unfair, and fail entirely to interpret or correlate the fundamental principles involved. If reliance be placed on clinical improvement alone as a criterion of the action of our remedies and the fluid changes disregarded, few, if any, permanent cures will be achieved, and sooner or later the patient's condition will relapse. There is as much reason for basing the efficiency of a therapeutic procedure on the changes in the biology of the fluid as there is in using the blood Wassermann as a test of the value of treatment of syphilis in general. If we were to discard the positive knowledge acquired in the past few years as a result of systematic examination of spinal fluids in syphilis, we should have vague ideas as to the time the fluid is infected, no clear conception of the difference between active and abortive tabes, and no method of differentiating early paresis from conditions that simulate it. Neurasthenic states, headaches, phobias, vague changes in mentality, crises, or impairment in the sexual functions are constantly overlooked or wrongly diagnosed by the pure clinician. Arteriosclerosis, chronic alcoholism, and diabetes may cause symptoms easily mistaken for the syphilitic syndrome.

The future of the syphilitic individual and the hope of anticipating or arresting the incurable degeneration is largely dependent on early and systematic examination of the spinal fluid.

[The therapeutic results of intraspinous injections of salvarsanised serum are too valuable to be discarded, or to allow the method to be discredited. We have recently seen a woman who had headache and a partial hemiplegia which persisted after eight intravenous injections. Examination of the spinal fluid showed 1,000 cells, positive Wassermann and globulin reactions. Intraspinous injection of salvarsanised serum gave immediate relief.—EDITORS.]

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Comparison in Mercurialized Serum and Salvarsanized Serum. A comparative study of the two serums leads Haller[8] to conclude that the irritating effect in the spinal canal of serum to which mercuric chloride has been added in the dose of 0.001 gm. is greater than that of 20 c.c. of salvarsanized serum separated from blood drawn thirty minutes after a dose of 0.6 gm. of salvarsan. The average effect of the laboratory findings in the spinal fluid from one dose of mercurialized serum is greater than from one dose of salvarsanized serum, but the unpleasant symptoms are more common following the former.

The greater irritation of the meninges from mercurialized serum prevents as rapid repetition of dosage as is possible with salvarsanized serum. Cases of general paresis, meningitis and cerebrospinal syphilis tolerate intraspinal treatment with mercurialized serum better than do cases of tabes dorsalis. It is particularly in cases of active syphilis of the meninges that the mercurialized serum is useful.

Eleven patients previously treated with salvarsanized serum were each given three or more intraspinal treatments with mercurialized serum, a total of thirty-eight doses. The effect on the Wassermann reaction, cell count and clinical symptoms was in every case equally as good as, if not better than, from the same amount of salvarsanized serum. The reactions in every case were more severe than with the salvarsanized serum.

Intraspinous Injection of Mercuric Benzoate. A new method for the intraspinous treatment of neural syphilis with mercurialized serum has been suggested by M. F. Lautman.[9] The method consists in pushing mercury to the point of tolerance, obtaining the blood serum, reinforcing this by the addition of a solution of mercuric benzoate in normal saline, removal of as much spinal fluid as can possibly be obtained by lumbar puncture, and injecting intradurally the serum preparation. The quantity of fluid injected should be less than the amount of spinal fluid withdrawn so as to create a negative pressure within the dural cavity.

(8) Archiv. Int. Med., June, 1917.
(9) New York Med. Jour., Dec. 30, 1916.

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To saturate a patient with the mercury give daily inunctions of 1/4 ounce of 50 per cent. mercurial ointment, supplemented by triweekly intramuscular injections of any one of the mercurial salts. These procedures are continued until the first evidences of ptyalism appear (foul breath, gingivitis and cramps), and then 30 c.c. of blood are removed by venipuncture. The rest of the technique is similar to that used in the Swift and Ellis method:

The blood is allowed to clot and the 10 or 15 c.c. of serum obtained are pipeted off and centrifugated to remove all the blood cells. One cubic centimeter of a solution of 1 grain of mercury benzoate in 25 c.c. normal saline is placed in a clean test tube and boiled. If on cooling this solution becomes turbid, it should be discarded and another cubic centimeter of the solution boiled up in the same tube. If this remain clear on cooling, the clear serum is added and the preparation is mixed well. It is then heated at 56° C. for half an hour and administered, by gravity, at body temperature.

Lautman has used the method in eighteen cases, although he reports but ten cases which completed the course of injections. The cases were unselected, and embraced almost all the forms in which neural syphilis manifests itself. The diagnosis in all the cases was based upon unmistakable clinical symptoms and a positive Wassermann, increased cell and globulin content in the cerebrospinal fluid. In all the cases, after from three to six injections the spinal fluid was rendered normal. In no case was there further deterioration during or after the treatment.

The Chemotherapy of Mercurial Compounds. An intensive and systematic study of the biologic properties of a number of mercury compounds is presented by Shamberg, Kolmer and Raiziss.[1] The bactericidal properties of various new mercurial compounds were determined by the correlated employment of the antiseptic and germicidal tests *in vitro* and by the use of the drug in experimentally infected animals.

The fact that a chemical substance is strongly germicidal in the test tube is no evidence that it will exert a

(1) Amer. Jour. Syph., January, 1917.

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demonstrable influence on the same organism in the living body. Such substances, however, are more promising for chemotherapeutic investigation than those which are inert. Vegetable organisms, such as *Staphylococcus aureus* and *B. typhosus,* are far more vulnerable to the action of mercury in the test tube than to salvarsan. Indeed, mercury possesses stronger bactericidal properties in the test tube than any chemical agent with which they experimented.

Salvarsan, however, is not devoid of germicidal effect, as it killed the staphylococcus in the dilution of 1 to 2,000 upon prolonged exposure. Salvarsan proved to be, by far, the most powerful trypanocide in the test tube known. By the method *in vitro-vivo,* it destroys trypanosomes in dilution as high as 1 to 40,000. Bichloride of mercury shows markedly inferior values in this respect.

In the test tube, salvarsan exhibits a greater destructive influence on *animal parasites,* and mercury a greater destructive influence on *vegetable parasites.* Salvarsan is a powerful trypanocide and a feeble bactericide; mercury is a powerful bactericide and a relatively feeble trypanocide. Trypanosomes and spirochetes appear to react chemotherapeutically in a similar manner. Medicaments which have a destructive effect upon the former likewise appear to exert a similar influence upon the latter. There is strong presumptive evidence that chemical substances which are capable of destroying trypanosomes in the animal's body exert a favorable effect in syphilis. The failure, however, of a chemical substance to destroy the parasites in experimental trypanosomiasis is, of itself, no proof that the medicament may not exert a favorable influence in syphilis.

The laboratory experiments of the authors on trypanosomes and spirochetes pointed to a greater selective affinity of salvarsan for the *Spirochaeta pallida* than is possessed by mercury. Mercuric chloride has a much greater organotropic effect than salvarsan; their experiments showed that mercury was fifty times more toxic for white rats than salvarsan.

A group of new organic mercury compounds was pre-

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pared which far transcend mercuric chloride in their bactericidal power in the test tube. One new compound has shown itself to be over thirty times more powerful in this respect, both by the Rideal-Walker and the "antiseptic" test. These new mercury compounds also exhibit a greater destructive influence upon trypanosomes than does mercuric chloride. Some of these compounds have shown a lower toxicity than mercuric chloride.

A New Mercurial Preparation. Of the various preparations in use, the salicylate of mercury, administered intramuscularly, has perhaps enjoyed the greatest popularity. Of late, however, the salicylate has fallen into disfavor owing chiefly to the unfavorable reports of Nelson and Anderson. These observers show that in a series of fifty unselected cases (mostly latent syphilis) the effect on the disease, as determined by the Wassermann reaction, was practically negligible. Schamberg, Kolmer and Raiziss have reported some very significant findings which support the assumptions of Nelson and Anderson. They have, as a result of very extensive experimental studies, calculated that the maximum rate of absorption of an insoluble salt of mercury is only 1.5 per cent., and that 50 per cent. of the mercury remains unabsorbed in the body even as late as six or seven weeks after injection. Best, while personally advocating the use of mercury salicylate, is unable, even by employing much larger doses than those generally used, to offer any convincing proof of any change in the Wassermann reaction, attributable to the salicylate alone.

It occurred to Lautman[2] that if one of the soluble organic mercurial salts were injected in an oily emulsion it might be absorbed more quickly than an insoluble preparation, and still not rapidly enough to produce the prompt mercurialization which results when large doses of a soluble salt in solution are employed. Working on this theory, he prepared an oily emulsion of 10 parts of mercury benzoate and 2 parts of quinine and urea hydrochloride in 100 parts of white liquid petrolatum. It is quite simply prepared by first grind-

(2) Med. Record, Jan. 18, 1917.

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ing up the quinine and urea hydrochloride with a little of the oil in a mortar and then adding with careful trituration small quantities of the benzoate and oil. A perfect emulsion is obtained, which can be easily aspirated through a twenty-gage needle. It is no more painful than any of the other preparations in use, and permits of giving three grains of the salt each week.

In twenty-five unselected and previously untreated patients the blood Wassermann was changed from a four plus to a negative in an average of eight weeks. The influence on the existing lesions was very favorable. The author does not intend to convey the impression that a negative Wassermann means that the syphilitic process has been cured or arrested, but the favorable effect on the Wassermann reaction would seem to indicate that the process has been temporarily controlled.

Painless Calomel Oil for Intramuscular Infection. A formula for an oily suspension of calomel which is said to be free from any pain when injected is given by Jacquot.[3]

	Grams.
Calomel (washed with alcohol and dried)	5
Guiacol	10
Camphor	10
Olive Oil (washed with alcohol and sterilized) g. s. ad	100 c.c.

This should be thoroughly shaken each time before using, and is injected deep into the gluteal muscle in the same manner as other insoluble mercurial suspensions.

Sodium Cacodylate in the Treatment of Syphilis. In spite of the attempts of several workers to disprove the claims made for sodium cacodylate as a powerful remedy in the treatment of syphilis, the drug is still extensively used by the general practitioner and by many specialists in the treatment of this disease. Yet Nichols, notably, by his work on rabbits, has proved that it is worthless as a spirocheticide.

To clear up the question as to its value, H. N. Cole[4] undertook the study of its action in a series of selected

(3) Ann. des mal. vén., 1917, p. 40.
(4) Jour. Amer. Med. Ass'n., Dec. 30, 1916.

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syphilitics in the wards at the Cleveland City Hospital. At first he gave a dose of 0.25 gm. intravenously, followed by a dose of 0.45 or 0.5 gm. every five days up to five or six injections. After one or two trials, however, he was convinced that he would have to use it either in larger doses or oftener to obtain results. The latter alternative was chosen, and it was employed at first every four days and later every three days.

The patients were together in wards, and it was not always possible to treat them as long as wished, because they took treatment into their own hands when results were not obtained. Otherwise they were all carefully studied, and collectively they showed most of the symptoms found with primary, secondary and tertiary syphilis; a few had involvement of the central nervous system.

Careful analysis of the results proved the contention of Nichols and others that sodium cacodylate is worthless as a spirocheticide; yet many physicians are depending on this drug today in the treatment of syphilis. Moreover, there is a widely advertised proprietary product on the market, *venarsen,* claimed to be of great value in the treatment of this disease, the main constituent of which is sodium cacodylate. And the dosage is not as large as Cole has employed.

At most, sodium cacodylate has perhaps a slight action on the papular and nodular syphilids, but in no case is it to be compared with even mercury and potassium iodide alone. The benefit is probably due entirely to the tonic action of the arsenic on the system.

In cases of syphilis with mucous patches it is worse than useless. In one case there was a drop in the spinal fluid cell count from 65 to 25, but the Wassermann and Noguchi tests remained positive, and two cases with cerebrospinal involvement showed practically no change. The dosage was to the limit of tolerance (0.5 gm. every three days), because routine urine examinations in several cases showed red cells and albumin, the one after four and the other after six injections. The routine positive blood Wassermann in all ten cases was in no instance changed to negative.

[The use of sodium cacodylate in the treatment of

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syphilis by the late Dr. J. B. Murphy served to fasten this therapeutic fallacy upon a large number of medical men, and it will be years before such a fallacy can be uprooted. We have recently seen a patient covered with pustular syphilides who had received a large number of sodium cacodylate injections without any benefit. One injection of arsenobenzol caused immediate healing. Depending upon sodium cacodylate in nervous syphilis is tragic because valuable time is lost.—EDITORS.]

Venarsen in the Treatment of Syphilis. This drug has been confused with salvarsan, and in many instances physicians have administered it under the impression that they were using American-made salvarsan. The preparation is frequently referred to as "Denver salvarsan." It is not salvarsan, however, but *sodium cacodylate.*

Brayton[6] has used the drug in a series of active syphilitics to determine its therapeutic value, and gives a report of the results obtained.

Six of the patients on whom treatment was begun did not return after the first two or three injections of the drug had been administered, because there was no noticeable improvement, and it was with difficulty that the patients were held to the treatment.

All individuals selected for the treatment showed 100 per cent. positive Wassermann reactions and active clinical manifestations of syphilis. In the ten cases reported, the patients were given from six to eight injections of *venarsen* at intervals of from two to five days. The initial dose in most cases was small. All subsequent doses, however, were the maximum, or 2.1 grams. Routine urine examinations were made prior to the injection of *venarsen.*

CASE REPORTS.

Case 1.—A. R., white female, with a primary sore, condylomata around vulva and anus, annular syphiloderms on the forearms, palmar and volar squamous syphilides, circinate lesions on the chin, mucous membrane involvement of mouth and throat; W. R. ++++. She was given one injection of *venarsen* (1.4 gm.) and seven injections (2.1 gm.) in sixteen

(6) Jour. Ind. State Med. Ass'n., September, 1917.

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days. No improvement was noticed in the cutaneous lesions and the mucous membrane lesions were slightly worse. All lesions disappeared rapidly under the use of *salvarsan*.

Case 2.—F. S., white male, W. R. ++++. Had had several attacks of recurrent iritis (luetic). He was given eight injections of *venarsen* (2.1 gm.) in a period of eighteen days. The condition became worse and remained so until the completion of the treatment. Under *salvarsan* the iritis rapidly disappeared.

Case 3.—L. N., colored female, with palmar and volar squamous syphilides, marked adenitis, circinate syphilides of face and chin; severe mucous membrane involvement of throat and mouth, deep ulcerations of uvula and tonsils, laryngitis and W. R. ++++. Six injections of *venarsen* were given in a period of sixteen days. The cutaneous lesions had extended and the throat was worse under the treatment. Rapid recovery occurred under the use of mercury salicylate and *salvarsan*.

Case 4.—N. W., male with severe recurrent mucous membrane syphilis of the mouth and condylomata around the anus. W. R. ++++. Six injections of *venarsen*, "triple strength," were given in a period of twenty-one days. The lesions became worse during the course of treatment. Rapid recovery occurred after the use of *salvarsan*.

Case 5.—S. T., male with severe mucous membrane syphilis of the mouth with deep ulcerations of both tonsils, laryngitis which made speech difficult, and dry, scaly, palmar and volar syphilides. W. R. ++++. Seven injections of *venarsen* were given in a period of eighteen days. The lesions became worse at the end of the treatment. The throat had become very painful and severe headaches had appeared. Rapid recovery occurred after the use of *salvarsan*.

Case 6.—B. B., male, with a chancre, mucous patches, a scaly macular eruption over the entire body and marked adenitis. W. R. ++++. Six injections of *venarsen* were given at three-day intervals. No improvement was noticed at the end of the treatment and *salvarsan* was instituted, after which the lesions rapidly disappeared.

Case 7.—E. D., male with recurrent ulcers of anterior tibial area of left leg and a periosteitis of the lower third of the tibia. W. R. ++++. Six injections of *venarsen* were given. No improvement was seen, and *salvarsan* was given, after which there was rapid recovery.

Case 8.—M. B., female, with an extensive mass of condylomata around the anus and vagina, marked inguinal adenitis, scar on vulva from primary sore, and a light macular eruption over body. W. R. ++++. Six injections of *venarsen* were given in a period of eighteen days. No improvement noted under *venarsen*. *Salvarsan* was given and the lesions rapidly disappeared.

Case 9.—O. D., male with scaly syphiloderms of palms and soles, rupial syphilides on body and ulceration of both tonsils.

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W. R. ++++. The patient was given six injections of *venarsen* (1.4 gm. and 2.1 gm. doses) in a period of fourteen days. No improvement was noticed. The lesions disappeared rapidly under the use of *salvarsan*.

Case 10.—M. K., female, white, with primary sore on the cervix, a light macular eruption over the body, adenitis and sore throat. W. R. ++++. *Treponema pallidum* present in primary sore. The patient was given four injections of *venarsen* in a period of nine days. On the eleventh day following the initial injection she returned to the dispensary complaining of extreme weakness and severe headaches. She stated that she had passed urine often and in small quantities for two days. The routine urine examination which was made before each injection of *venarsen* showed: specific gravity, 1.025; albumin, positive; microscopic, red blood cells and red blood cell casts.

She was taken to the hospital immediately, where she recovered in seven days from the nephritis. No improvement was seen from the treatment of *venarsen*. The eruption was more pronounced and new lesions had appeared in the mouth. *Salvarsan* was instituted following which there was prompt recovery.

Brayton considered the following conclusions justified:

1. *Venarsen is worthless in the therapy of syphilis.*
2. Venarsen has absolutely no spirocheticidal properties, disproving the claim of the manufacturers.
3. Often repeated injections of the maximum dose do not show any favorable effect on the Wassermann reaction.
4. A venous sclerosis was produced in each case in which the drug was administered, due to chemical irritation.
5. Syphilitic lesions of the mucous membrane and cutaneous surfaces progressively became worse during the course of *venarsen* treatments.
6. *Venarsen* is a dangerous preparation capable of producing a severe nephritis.

Treatment of Syphilis with Galyl. Of the arsenical preparations closely allied to salvarsan there is one, galyl, which has received but scant notice in the literature in this country, but which has been used extensively in France. This drug was discovered by Mouneyrat and was given the name of galyl after Galen, who first de-

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scribed the properties of arsenic. Galyl is a yellow or greyish-yellow powder containing 35.3 arsenic and 7.2 per cent. phosphorus. It is odorless, tasteless and insoluble in water, ether, alcohol and benzene. It is, however, readily soluble in a dilute solution of sodium carbonate, forming a yellow or yellowish-brown liquid. The ampoules in which galyl is dispensed contain a small quantity of sodium carbonate so that solution takes place readily upon the addition of distilled water. It is, therefore, as easily prepared for injection as neosalvarsan.

Loyd Thompson[7] has given sixty injections to twenty-eight patients. He makes no attempt to draw definite conclusions from this small number of injections, but wishes to bring the drug to the attention of the profession. The author states that the results with galyl seem to be as good as with other arsenical preparations, and in his limited experience there has been no severe reaction following its use.

Vanadium in Syphilis. A valuable and comprehensive study, both pharmacologic and clinical, of vanadium and its various salts has been made by Proescher and Seil of Pittsburgh, and Stillians[8] of Cook County Hospital, Chicago. The effect of the salts was determined upon plant and animal life, upon bacteria and upon experimental trypanosomiosis and spirochetosis.

It was found that the simple vanadium salts would suppress the multiplication of *Typanosoma brucei*, or temporarily inhibit the course of the disease in animals. Complete sterilization, however, could not be accomplished. Sodium tetravanadate combined with arsacetin gave complete sterilization in 92 per cent. of the animals.

It was also found that the vanadium salts have a marked effect on *Spirochaeta pallida* and that they are capable of curing experimental syphilis in rabbits.

In human syphilis it was demonstrated that the injection of 10 to 20 mg. of sodium tetravanadate caused a disappearance of *Spirochaeta pallida* in 24 to 48 hours. The syphilitic lesions cleared up in two to six days

(7) Amer. Jour. Syph., 1917, p. 665.
(8) Ibid., 1917, p. 847.

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after the injection of 10 to 140 mg. On account of the toxicity of sodium tetravanadate the use of this salt was abandoned in favor of sodium hexavanadate.

The moist secondary lesions invariably show a rapid improvement whether treated intravenously or intramuscularly. The dry lesions did not yield so readily but they showed improvement in about a week. Mucous patches, moist papules and flat condylomata were cleared up in from three to thirteen days.

The appearance of albumin and casts in the urine, or of anorexia or slight nausea, indicate intolerance to the drug, and call for intermission in the treatment. These symptoms may be delayed until the second day after injection, and therefore a three-day interval should be allowed between injections.

Failure of Present Methods of Treatment in France. The creation of a *"centre vénéréologique"* (*vide* page 130) in each of the French armies for the care of all cases of venereal disease has made it possible for Carle and Carrère[8] to gather data on the frequency of recurrences of syphilitic lesions both in those soldiers who had received treatment prior to mobilization, and also in those who had been treated since entering the army.

It is obviously impossible to get accurate statements from patients as to the particular arsenical preparation injected on previous occasions. Furthermore, there were histories of many attempts to inject patients both intravenously and intramuscularly, which failed and therefore the exact amount injected can not be determined. It is evident, however, that lesions recur in a great many patients who have had what has been thought by many workers to be sufficient treatment. A number of cases showing active lesions were seen in which there was a history of five to ten intravenous arsenical injections and twenty to fifty mercurial injections. The authors classify the material as follows:

Class I.—Patients appearing to have received treatment which, if not intensive, was at least sufficient.

A—Cases without lesions..... 4.7%
B—Cases with active syphilis..... 6.1%

(8) Ann. de derm. et syph., 1916, p. 277.

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Class II.—Patients who received insufficient treatment.
A—Cases treated by injections.....40.7%
B—Cases treated by mouth 11.8%

Class III.—Patients in whom syphilis had not been previously suspected.
A—Recognized and treated late in the course of the disease 14.2%
B—Never recognized and never treated....22.2%

In group A of the first division were (1) men who were seen for dermatoses other than syphilis; (2) men who had been sent by regimental surgeon for examination; and (3) men who had submitted themselves for examination. This was the smallest of all the groups.

Group B, Class I, was slightly larger, numerically, but nothing but very mild recurrences were encountered. The results, however, indicate that the intensity and duration of routine treatment must be increased.

A study of Class II convinces the authors that the German press agents of salvarsan did a great harm in the early days of the marketing of the product by arousing hopes in the minds of both physician and laymen that *one* injection of that drug is sufficient to effect a cure. Many soldiers were seen who had been given one injection and who had received no further attention for the reason that they had supposed a permanent cure had resulted from the one injection. The cases in this group serve to emphasize three points: (1) The importance of early treatment and the importance of not considering this treatment curative no matter how intensive it may have been; (2) the necessity of continuing treatment for long periods (2 or 3 years) at regular intervals regardless of the method employed, and (3) the necessity of keeping the patient under prolonged medical observation.

The cases in Class III resulted from failure on the part of the patient to seek medical advice, or failure on the part of the physician to make a correct diagnosis. The cases in this group are a demonstration of how imperative it is that the clinician be qualified properly to interpret the serological reactions, and to recognize the cutaneous lesions of syphilis. They confirm a say-

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ing of Fournier, *"que l'on ne songe jamais assez à la syphilis"*—one should always bear syphilis in mind.

[The therapeutic principle of intensive arsenical treatments with short periods of rest between series was first advocated by Viennese syphilographers, but later abandoned by them because of the unfortunate sequelae. Last year this method was strongly urged by Pollitzer (Practical Medicine Series, Vol. IX, 1916, p. 194), who termed it the method of "fractional sterilization." During the past year we have been able to get much better results in this way than ever before. Cases having a positive Wassermann reaction, which have resisted all treatment, have yielded to three intravenous injections given daily or every other day. In some cases it has been necessary to give several series of such intensive treatment. When seen early, cases yield readily. Caution must be exercised in the proper selection of the cases, and of the arsenical preparation. We have found *arsenobenzol,* which is now produced under license from the Federal Government by the Dermatological Research Laboratories of Philadelphia, to be the least toxic of any drug we have thus far used.—EDITORS.]

Studies on Absorption of Mercury. In a previous publication Wile and Elliott[1] detailed experiments bearing on the mode of absorption of mercury in the inunction treatment of syphilis. In the present paper they repeat the experiments with various mercurial salts of low vapor pressure in order to determine whether such salts could be absorbed through the skin, under conditions which did not permit of their volatilization.

In brief, the method of detection of mercury embodies the use of copper dust in an acid solution of the suspected material. The mercury is taken up to its last trace by the copper dust. The latter is then collected, dried and heated in the distal end of a bulb-tube. The mercury is thus driven off and deposited as an amalgam on a small particle of dental gold leaf. By means of this test they have been able to detect most minute quantities of mercury in solution.

Their preliminary experiments led to the belief that blue ointment or unguentum hydrargyri, and calomel

(1) Jour. Cut. Dis., September, 1917, p. 594.

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ointment of equal mercurial content, representing forms of mercury having a high vapor pressure, were far more readily absorbed and eliminated in larger quantities when anointed on the skin, than any other salts employed.

In the present series of experiments they attempted a comparison of the absorbability and elimination, particularly of calomel ointment and blue ointment. It was thought that if calomel were as readily absorbed and as readily eliminated as the blue ointment, one might conclude that its therapeutic effect would be equally as rapid. In this event its greater cleanliness might justify replacing the blue ointment in our therapeutic armamentarium. They also attempted to determine not only the presence of mercury from parallel inunctions of mercury ointment and calomel ointment in the urine, but investigated further the various body fluids, such as the stomach contents, the saliva, the blood, the milk, and the spinal fluid.

Experiments on the blood showed that mercury is eliminated into the blood-stream more rapidly in the case of blue ointment than in the case of calomel. As an incidental experiment they determined with great readiness the presence of mercury in the blood, following injections of salicylate of mercury, bichloride of mercury, and succinimide of mercury. In the case of the sublimate, mercury was found after the third injection. In the case of the other two salts, both had been given a longer time, although mercury was probably present in the blood before they tested for it.

In their experiments on the spinal fluid they attempted the detection of mercury in many different experiments following inunction of both calomel and blue ointment, and following injections of mercury salicylate, succinimide, and bichloride. In no case were they able to detect the faintest trace of mercury in the spinal fluid. Believing that perhaps the amount of fluid tested was too small, they collected fluid from several different cases that had been taking mercury in various forms for a long period of time. This experiment likewise proved negative. They were able, furthermore, to test the spinal fluid of a patient who died

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of mercurial poisoning from ingestion of sublimate. The spinal fluid in this case also failed to reveal the presence of mercury.

The milk from various nursing women was tested following their inunction with both blue ointment and calomel. In both cases mercury in appreciable quantity was found as soon as tested for; that is, after one week of inunctions, and undoubtedly would have been shown to be present earlier had there been the opportunity of testing for it. To avoid the possibility that the milk had been contaminated by the skin, they placed nursing women on the injection treatment and found mercury in the milk forty-eight hours after injection with the bichloride. From this experiment it is evident that mercury is eliminated in very appreciable quantity by the lactiferous glands.

It has long been known that mercury is eliminated through the salivary glands and that its presence gives rise to salivation in cases of overdosage of mercury. They investigated the saliva of patients receiving inunctions of both calomel and blue ointment and were able to detect mercury, although not in strikingly large quantities, in both instances. One case in which calomel ointment was used in connection with wet dressings of sublimate on an open syphilitic ulcer, yielded a very positive result in the saliva in the absence of any evident stomatitis or salivation. It may thus be concluded that the salivary glands excrete mercury even in the absence of excessive glandular activity.

In washings from the stomach the authors were able to detect mercury following inunctions of both calomel and blue ointment. In both cases, however, the tests were made after several inunctions had been given. It seems not unlikely that it would have been found earlier if they had had the opportunity of making the tests.

Although they have no definite data as to the relative rapidity with which mercury may be determined following inunctions with calomel and blue ointment in the case of other body fluids, they have found definitely that in the case of calomel, the elimination in the urine is much slower than it is with blue ointment.

With regard to the relative therapeutic value of calo-

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mel and blue ointment, they are not prepared to make a definite statement at this time. From observation and from communications from others who are using calomel in the form of inunctions, it would seem that its therapeutic effect stands favorable comparison with the therapeutic effect of the blue ointment.

[Quite frequently a patient will be encountered who is unable to tolerate mercury either by mouth or by intramuscular injections. Furthermore, owing to close contact with other members of the family it is difficult or impossible to use unguentum hydrargyri because of its staining properties. In such cases 50 per cent. calomel ointment may be employed without exciting suspicion, and with excellent therapeutic results.—ED.]

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